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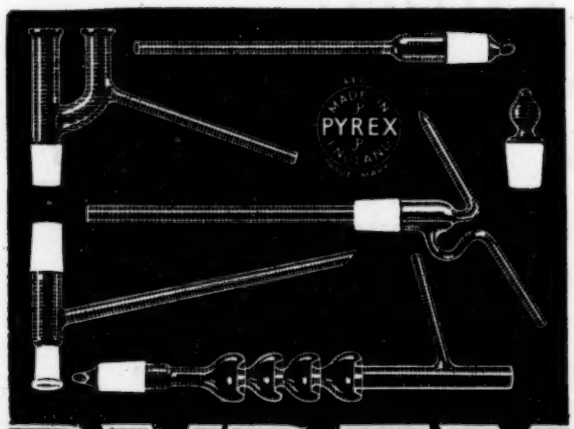

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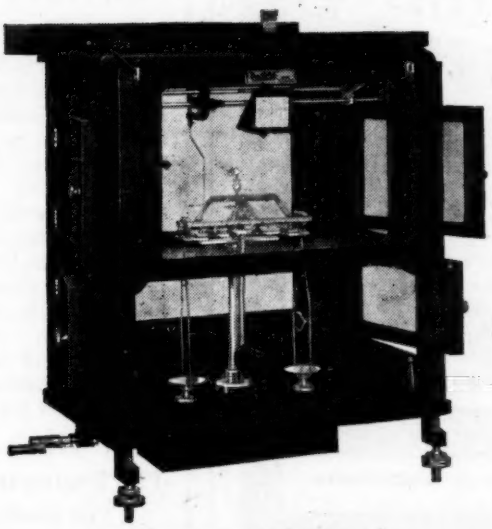

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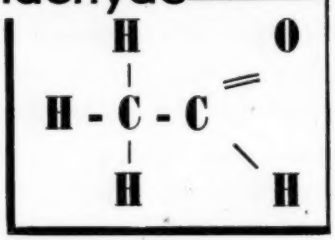

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again at a suitable concentration of the solid. Green, at a time when the phenomenon of thixotropy was hardly known, published striking photomicrographs of plastic pastes of zinc oxide formed by suspensions in kerosene, which showed the zinc oxide particles to be coagulated. When poppy seed oil was added as a dispersing agent, the same particles were independent and dispersed. They are good examples of the state of the particles in a thixotropic and in a dilatant system.

" Our knowledge of the forces acting between the particles and causing these phenomena is not yet sufficiently advanced to allow me to state concisely the processes involved. Only a few points may be mentioned. The geloids in thixotropic sols and gels are closely related to the tactoids, *i.e.*, double refracting groups of oriented particles formed spontaneously in concentrated sols containing non-spherical particles, and to the coacervates as defined by Bungenberg de Jong, *i.e.*, liquid coagulates of hydrophilic sols containing one or more kinds of colloidal particles. In geloids, tactoids, and coacervates, the colloidal particles are very far apart, up to many μ. It is, therefore, improbable that the attraction between the particles is due to van der Waals forces, which act over smaller distances; an attraction due to electric forces is more probable. The possibility has been considered that both attractive and repulsive forces between the particles may be of electric origin. But this concept is perhaps not easily reconciled with the fact that the forces between the particles may be markedly specific. Vanadium pentoxide, as well as benzopurpurin sols, form tactoids which carry a negative electric charge. In a mixed sol of the two, under proper conditions, both kinds of tactoids may be formed side by side, containing only vanadium pentoxide and benzopurpurin particles respectively. These two kinds of tactoids can be distinguished, because those of vanadium pentoxide are positively, those of the dye negatively, double refracting. The very specific behaviour of some ions when producing autocomplex coacervates must also be mentioned in this connection.

" The non-spherical shape of the colloidal particles strongly favours thixotropy. But the opinion, which has been occasionally expressed, that non-spherical shape is an indispensable factor for thixotropy is not correct. Thixotropic systems are known whose particles hardly deviate from the spherical shape, *e.g.*, pastes of intact starch grains in organic liquids. . . ."

There can be no doubt that Freundlich's researches on the viscosity and elasticity of colloid systems and the phenomena of thixotropy must be regarded as another of his major contributions to the advance of colloid science and also to that of the modern subject of rheology.

Having obtained (by means of a special grant from the Rockefeller Foundation) a Siemens piezo-electric quartz disc oscillator, Freundlich began about 1930—31 a series of investigations on the effects of supersonic (ultrasonic) vibrations, his chief collaborators in this field of work being K. Sollner, C. Bondy, and F. Julius Burger. It was shown that thixotropic gels, like those of iron oxide, are liquefied by ultrasonics of sufficiently high energy, and that a thixotropic decrease of the structural viscosity of concentrated colloid solutions can also be produced. Another striking effect is the dispersion of mixtures of liquids such as benzene and water, emulsions being formed. These " destructive " actions were shown to be due to the phenomenon of *cavitation*. The high-frequency waves produce periodic dilatations and compressions, and if the dilations be intense enough the liquid is caused to " tear," cavities containing vapour being formed. When such cavities pass into the regions of high pressure they may suddenly collapse with almost explosive violence, leading to very high local concentrations of energy. This theory of cavitation was confirmed by the fact that in a vacuum or under sufficiently high external pressure the effects mentioned are not observed. No doubt in these cases the vapour-filled cavities either do not collapse or are not formed.

In emulsions and suspensions of suitable concentration, stationary ultrasonic waves were observed to produce periodic accumulations of the dispersed particles at the nodes or antinodes according as the particles are lighter or heavier than the surrounding liquid. Coagulation may occur where this accumulation takes place. Another interesting effect caused by very weak ultrasonic waves was observed; rod- or plate-like particles of a suspension are oriented with their long axes vertical to the direction of the energy-flow. It was an investigation (with K. Sollner) of the effects produced on biological systems by ultrasonic vibrations which attracted Freundlich to the special study of this field of research.

This account of his investigations in many parts of colloid science would be incomplete without at least a passing reference to his many published papers (1911—1933) on the chemistry and chemical kinetics of the transformation of halogen-substituted alkylamines into heterocyclic compounds (cyclic imines). Of interest in this connection was his demonstration (with Salomon) that adsorption on charcoal increases the " life " of β-chloro-β-phenylethylamine, this " negative " catalytic action being probably or possibly due to an oriented adsorption of the molecules.

Freundlich was in no sense a mathematical physicist. He left the rigorous—or the attempted rigorous—treatment of the problems he investigated to others. His success as an investigator was due to his deep interest in phenomena as such, his excellent intuition and imagination, and his ability to correlate phenomena and perceive analogies between processes sometimes belonging to very different fields of science. Apart from the great effect of his researches in opening up and stimulating research in many different fields of colloid science, his famous book on *Kapillarchemie* has had a profound influence on the work of many investigators, both young and old. The latest German edition of this book in two volumes (Leipzig, 1930 and 1932) is a vast production which must have demanded immense industry on the part of the author. It is still an indispensable " reference book " for all active workers and all seekers in the lore of colloid and interfacial phenomena, though the author's

desire to make his book all-comprehensive has had the effect of making it rather cumbersome and perhaps in some respects not sufficiently selective and critical.

Freundlich's enthusiasm, wide knowledge and understanding of his subject, and his modest, cheerful, and kindly temperament made him a University teacher of the best type and a never-failing guide and friend of his many research students and collaborators. There was nothing of the drill sergeant or formal bureaucratic organiser about his methods. Both in Braunschweig and Berlin-Dahlem his work and influence in the conduct of the scientific *Colloquium* had a most valuable and inspiring influence on the young investigators who assembled weekly to discuss their own and others' researches. There is no better testimony to Freundlich's success in winning both the affection and the respect of his students and collaborators than the friendly nicknames bestowed on him. It is related that in Dahlem he was known as the " Gentle Shepherd," and in Minneapolis as " Uncle Herbert." When he came to us in London he never uttered a complaining word, although the small space in the laboratory that could be allotted to him must have been in sharp contrast to that in Dahlem. On the contrary, he exerted himself to be helpful in many ways, and although there must have been sorrow in his heart he kept a cheerful countenance to the world.

It is remarkable how many investigators owe the direction of their subsequent researches to the initial influence of their collaboration with Freundlich. He was always most unselfish in giving advice and help to those who sought it, and there must be many who never worked in his laboratory who owe much to him.

Freundlich was always moderate and critical in the statement of his results, and shunned speculative theories. Perhaps his only venture into this land of often unfulfilled promise was his paper on the " Occurrence of a mutation from the standpoint of probability," published in *Die Naturwissenschaften* in 1919.

Although devoted to research in pure science for its own sake, he was always anxious to show the value of applying the results to the explanation and improvement of industrial processes. Thus already in 1904 he published papers with F. Emslander on surface influences and phenomena in brewing, whilst in later years he did much technical work on rubber latex, and the rubber industry in general, and pointed out the bearing of thixotropy on the processes of the oil and paint industries. He was also interested in colloid phenomena in the industry of petroleum and in adsorption and interfacial actions in the processes of detergency and ore flotation. He well understood the meaning and importance of that great reversible equilibrium, Science $\rightleftharpoons$ Industry.

Freundlich was a man of highly cultivated mind, tolerant spirit, and strongly artistic temperament. When such a man puts his faith in the power of experiment and reason to unravel some part at least of the mystery that surrounds and dwells within us, the cause of civilisation advances, even though it be but a little way, against the dark forces of blind unreason and savage prejudice that always seek to thwart it. We, his many friends in many lands, who live to mourn the passing of Herbert Freundlich, will keep his memory green.

In the writing of this memoir I have received most valuable assistance from Dr. Karl Sollner. Indeed, without that freely given help, the writing of it would have been well-nigh impossible. For many details concerning Freundlich's earlier life and career I have received great help from his sister, Mrs. Elizabeth Wardale, and his brother, Professor Erwin Finlay-Freundlich. I am also indebted to Dr. E. Heymann of Melbourne University for some valuable opinions. To all these friends I desire to express my most sincere thanks.

F. G. DONNAN.

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135. *The Crystal Structure of Rubber Hydrochloride.*

By C. W. BUNN and (MRS.) E. V. GARNER.

Rubber hydrochloride $[-(CH_3)_2{\cdot}C(CH_2)Cl-]_n$ is of interest in the study of the stereochemistry of long-chain polymers. The form of the chain has previously been predicted on the basis of (*a*) a knowledge of the identity period and (*b*) the assumption that the bonds of linked carbon atoms are everywhere in staggered positions.

The crystal structure has now been determined by *X*-ray methods. The unit cell is monoclinic (pseudo-orthorhombic) with $a = 5{\cdot}83$, $b = 10{\cdot}38$, $c = 8{\cdot}95$ A.; $\beta = 90°$. Two long-chain molecules pass through this unit cell. The symmetry of the arrangement is $P2_1/c$. The predicted chain form (symbolised A_2BA_2C), in which the principle of staggered bonds is obeyed, is found to be correct.

The relation between the molecular structure and the physical properties (particularly the melting point) is discussed.

" RUBBER hydrochloride," the crystalline substance made by addition of hydrogen chloride to rubber, is of interest for two reasons. First, the periodicity along the fibre axis of drawn specimens (Gehman, Field, and Dinsmore, *Proc. Rubber Tech. Conference*, 1938, p. 961) indicates that the carbon chain has not the simple plane zigzag form found in the paraffin hydrocarbons (Bunn, *Trans. Faraday Soc.*, 1939, **35**, 482), but is somewhat shortened by folding. There is similar evidence that several other chain polymers also have folded chains (Fuller, *Chem. Reviews*, 1940, **26**, 143); the elucidation of the geometry of such molecules would form a useful contribution to our knowledge of the stereochemistry of carbon compounds in general and chain polymers in particular. Rubber hydrochloride appeared to be a suitable substance for crystallographic investigation from this point of view: it gives a well-defined *X*-ray diffraction pattern. Moreover, a prediction of the chain form has been made on the basis of a knowledge of the periodicity and the use of a hypothesis which has been called the principle of staggered bonds (Bunn, *Proc. Roy. Soc.*, 1942, *A*, **180**, 67); the determination of the structure by *X*-ray methods forms the first test of the validity and usefulness of this hypothesis.

Secondly, rubber hydrochloride is interesting on account of its physical properties. Unlike rubber itself,

it is crystalline at room temperature, " melting " at about 115°. The present work on its crystal structure forms part of a programme of research being carried out in this laboratory, being a contribution to the attempt to understand the physical properties of chain polymers in terms of molecular structure.

Chemical Structure.—The chemical structure of rubber is

$$[-CMe{=}CH{-}(CH_2)_2{-}CMe{=}CH{-}(CH_2)_2{-}]_n.$$

Hence, on the assumption that hydrogen chloride adds on according to Markownikoff's rule, the chemical structure of rubber hydrochloride is expected to be

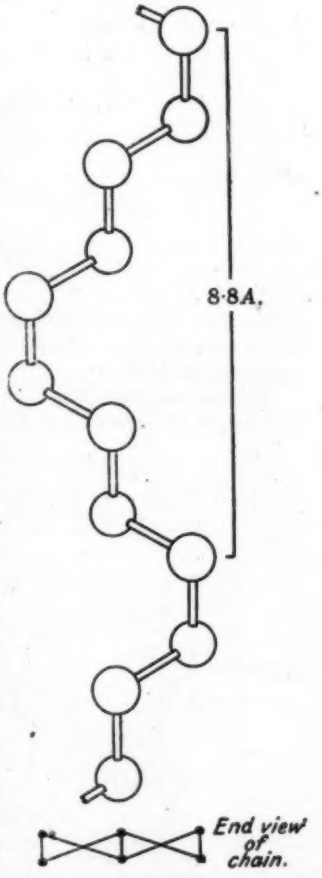
$$[-CClMe{-}CH_2{-}(CH_2)_2{-}CClMe{-}CH_2{-}(CH_2)_2{-}]_n$$

Experimental Details.—The crystal structure was deduced from *X*-ray diffraction photographs taken with copper radiation filtered through nickel foil to remove the *K*-β wave-length. Two types of photograph were used—the usual fibre photograph, with the beam perpendicular to the fibre axis, and also photographs taken while the fibre axis was oscillating with respect to the beam. In both cases the spots were recorded on a cylindrical film, for the sake of obtaining the maximum angular range of reflections. The second type of photograph yielded reflections from planes perpendicular or nearly perpendicular to the fibre axis, some of which do not appear on the first type of photograph.

The best orientation of crystals in the specimens was obtained by drawing out a thin strip at 90° and allowing it to cool while still extended. The normal fibre photograph shows 24 reflections, the intensities of which were estimated visually. Attempts to obtain a double orientation by rolling strips of material failed; it was therefore not possible to obtain direct information on the orientation of crystal planes; interpretation rests simply on the positions of the spots on the photographs.

Unit Cell Dimensions.—The cell spacing along the fibre axis can be measured directly from the layer-line separation on the normal fibre photograph and is found to be 8·95 A. The cell dimensions in the directions perpendicular to the fibre axis cannot be measured directly, but all the spots on the photograph are found to fit a rectangular cell with $a = 5{\cdot}83$, $b = 10{\cdot}38$, c (fibre axis) $= 8{\cdot}95$ A. From these dimensions, and the reported density of 1·193 g./c.c. (Gehman, Field, and Dinsmore, *loc. cit.*), the number of $^-CMeCl^-(CH_2)_3^-$ units in the cell is found to be 3·8. There are evidently four of these units in the cell. On this basis, the true density of a single crystal is calculated to be 1·255. The lower density of the bulk material is presumably due to the presence of a certain amount of amorphous material, which, being inefficiently packed, would be expected to have a lower density than the crystals. Specimens of long-chain polymers usually have somewhat low densities for this reason. In the case of rubber hydrochloride, there is a second reason why the amorphous material is expected to have a low density; hydrochlorination in the specimens examined was not complete, the chlorine content being only 29·3% (Calc. for C_5H_9Cl: Cl, 34%), and unreacted molecules or sections of molecules, which would be lighter than the rest, are expected to form part of the amorphous material.

FIG. 1.
Chain type A_3BA_3C.



Space Group and Parameters.—The space-group symmetry of single crystals can usually be determined unambiguously by observing which types of *X*-ray reflection are systematically absent, and combining this information with that provided by crystal morphology and pyro- or piezo-electric properties. The problem is more difficult in the case of polymers, since these substances cannot be obtained in the form of single crystals; not only can no information be derived about crystal habit and pyroelectric properties, but frequently the information about absent reflections is ambiguous owing to the overlapping of spectra. This means that usually a number of different space groups must be considered. To shorten the search for the correct arrangement, it is desirable to use external evidence, if this appears to limit the possibilities.

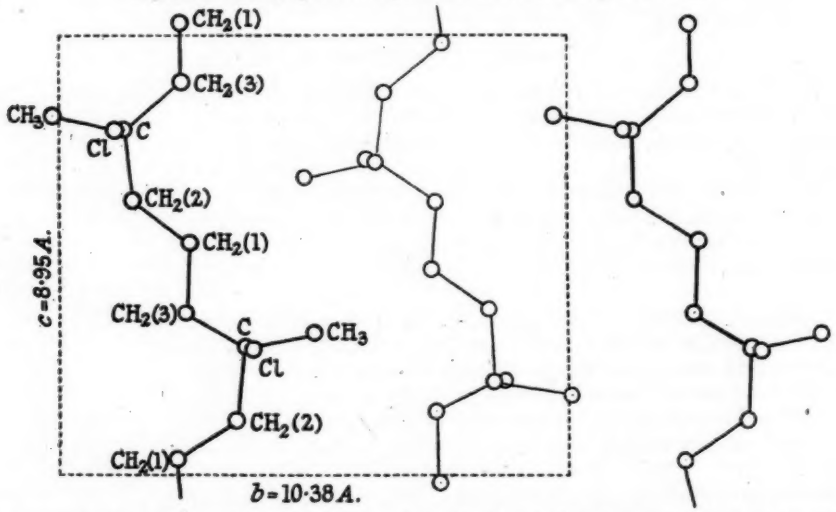
For rubber hydrochloride, it is found that, among reflections which can be uniquely indexed, the only systematic absences are the odd orders of $0k0$, and also $h0l$ reflections having l odd; if these absences are not accidental, it appears that there is a screw axis parallel to b, perpendicular to which is a glide plane with translation $c/2$. Since the cell is rectangular, the symmetry would be expected to be orthorhombic; but there is no orthorhombic space group giving the particular combination of absences mentioned; in fact, the absences indicate the monoclinic space group $P2_1/c$. There remains, however, the doubt whether some of the " absent " reflections really have small intensities but are too weak to be detected on the photographs; in view of this doubt, it is necessary to consider the stereochemistry of the molecules themselves.

The chain form of rubber hydrochloride molecules has already been predicted (Bunn, *loc. cit.*, 1942, *A*, 180, 67); it being assumed that the bonds of singly-linked carbon atoms are staggered, the only chain form

which has approximately the identity period found in rubber hydrochloride (8·95 A.) is the form A_3BA_3C (Fig. 1). This chain form is also consistent with the probable chemical linking in the molecule (Markownikoff's rule being assumed); the section $-CH_2-CH_2-CH_2-$ would be likely to have the plane zigzag chain (an *A* sequence) as in polyethylene; only at the >CMeCl unit is there likely to be a *B* or *C* link. The chain A_3BA_3C has a

FIG. 2.

Crystal structure of rubber hydrochloride seen along the a *axis.*

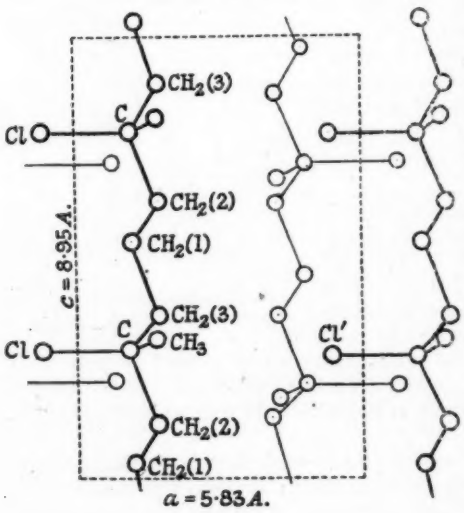


glide plane with translation $c/2$, and the presence of methyl and chlorine substituents (provided they are in equivalent stereo-positions) does not affect this symmetry; the space group $P2_1/c$ is thus consistent with the suggested chain form.

On the assumption, then, that this monoclinic space group and the suggested chain form are correct, it remains to determine the atomic parameters by calculation of the intensities of the reflections. Since in the identity period of the molecule there are two $[-CMeCl-(CH_2)_3-]$ units, and the number of such units in the cell is four, there must be two chain molecules passing through the cell. The orientation of these molecules is fixed: the glide plane is perpendicular to the *b* axis. There are two alternative positions for the methyl and chlorine substituents; either the chlorine is on bond *p* (Fig. 4), while the methyl is on bond *q*, or the reverse may be true. The decision that the former is correct, as well as the relation of the chains to the screw axis and the precise atomic parameters, rest on calculations of the intensities of all the reflections. Satisfactory agreement between observed and calculated intensities is attained if it is assumed that the atoms occupy the positions given in Table I. The intensities are given in Table II. The predicted chain structure and the space group $P2_1/c$ are evidently correct.

FIG. 3.

Crystal structure of rubber hydrochloride seen along the b *axis.*



If the co-ordinates of any atom are x, y, z, there are corresponding atoms in the same chain at $x, \frac{1}{2}-y, \frac{1}{2}+y$, and in the second chain at $\bar{x}, \bar{y}, \bar{z}$ and $x, \frac{1}{2}+y, \frac{1}{2}-z$.

Description of Structure.—Figs. 2, 3, and 4 show projections on planes perpendicular to the three axes of the crystal. Fig. 5 shows one repeating unit of the rubber hydrochloride molecule. The predicted chain form is definitely confirmed. The results of this work thus demonstrate the usefulness of the principle of staggered bonds, on which the prediction was based, and also provide yet another example in which the principle is obeyed.

TABLE I.

Atomic parameters in fractions of unit cell edges.

	x.	*y.*	*z.*		*x.*	*y.*	*z.*
CH_2 (1)	0·204	0·238	0·032	CH_3	0·281	0·51	0·32
CH_2 (2)	0·293	0·356	0·126	Cl	−0·11	0·39	0·283
C	0·195	0·371	0·285	CH_2 (3)	0·293	0·252	0·37

TABLE II.

Comparison of observed and calculated intensities.

Index.	Intensity. Calc.	Obs.	Index.	Intensity. Calc.	Obs.	Index.	Intensity. Calc.	Obs.	Index.	Intensity. Calc.	Obs.	Index.	Intensity. Calc.	Obs.
010	0	0	320	0	0	051	0	0	212	34	vw	203	0	0
100	74	m	060			151			042	49	w	213		
020	231	vs	250	21	vvw	301	64	m	222			043	31	vvw
110			330			241			142	91	w	223		
120	0	0	160			311			232	18	0	143	2	0
030	0	0	011	14	0	321	8	0	052	0	0	233	0	0
130	190	s	101	0	0	060	47	vvw	152	18	0	053	0	0
200			021	338	vs	251			302			153		
210	34	m	111			331			242			303	42	vvw
040	14	0	121	107	m	012	20	0	312			243		
220			031	4	0	102	176	s	322	2	0	313		
140	34	w	131	10	0	022			103	0	0	*001	0	0
230	32	vw	201			112			023	82	vw	*002	157	s
050	0	0	211	48	w	122	5	0	113			*003	46	m
150	79	m	041	2	0	032	0	0	123	100	w	*013		
300			221			132	20	vw	033	1	0	*004	23	w
240			141	7	0	202			133	22	0	*104		
310			231	10	0									

* The intensities of these planes were estimated independently from a photograph taken with the fibre axis horizontal and oscillated about a vertical axis between 45° and 90° to the *X*-ray beam.

No corrections have been made for thermal vibrations of the atoms. For this reason, the observed intensities should fall away from the calculated intensities with increasing angle of reflection. This does, in fact, occur.

No great accuracy can be claimed for the values of the atomic parameters on account of the small amount of information on which they are based. The possible errors of the parameters also vary with the diffracting power of the atoms concerned. By displacing the atoms by definite amounts and calculating the intensities, we assess the possible errors at about 0·02 A. for chlorine and 0·05 A. for carbon atoms.

FIG. 4.

Crystal structure of rubber hydrochloride seen along the c *axis.*

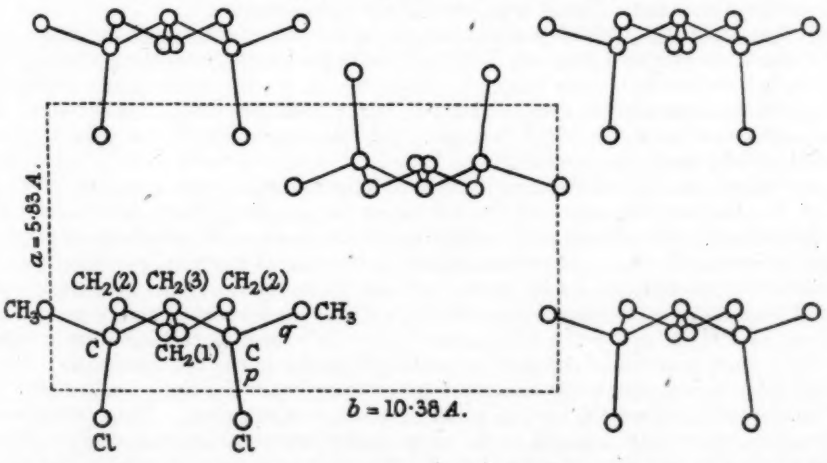
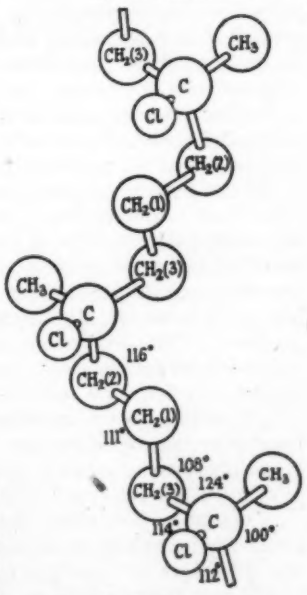


FIG. 5.

Geometry of the rubber hydrochloride molecule.

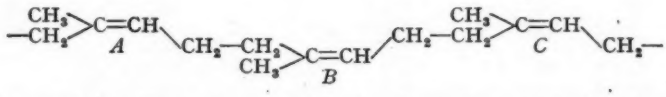


Within the above limits of experimental error, all C–C distances have the normal value of 1·54 A., and the C–Cl distance is 1·79 A. (compare 1·77 A. in polychloroprene). The nearest distances between carbon atoms in different chains vary from 3·89 A. to 4·11 A., and between carbon atoms and chlorine atoms in different chains from 3·76 to 3·83. None of the bond angles between carbon atoms in the chains differs by more than 4° from the value of 112° found for a paraffin chain (Bunn, *Trans. Faraday Soc.*, 1939, **35**, 482). The angles made by the C–CH_3 bond with the two adjacent C–CH_2 bonds, however, deviate considerably from the normal value. The angle $CH_2(3)$–C–CH_3 (Fig. 6) is 124°, and the angle $CH_2(2)$–C–CH_3 is 100°. The apparent reason for these abnormal angles is the repulsion of the CH_3 group by $CH_2(1)$; this has the effect of enlarging the angle $CH_2(3)$–C–CH_3 and at the same time diminishing the angle $CH_2(2)$–C–CH_3. An exactly similar distortion of the methyl group from the "ideal" position has been found in rubber (Bunn, *loc. cit.*, 1942), and this too can be attributed to the same cause.

The mode of packing of the molecules shows clearly the reason why the angle β (which in the monoclinic system is not fixed by symmetry) is in this crystal 90°. The chlorine atom of one molecule (Cl′ in Fig. 3) fits

into the hollow formed by groups CH_3, $CH_2(2)$, and $CH_2(3)$ attached to carbon atom C of the molecule in front, *i.e.*, the next molecule along the *a* axis. This packing ensures that the *z* co-ordinate of Cl′ is about the same as that of C, and since the carbon–chlorine bond is at right angles to the chain axis, the angle β must necessarily be approximately 90°.

Stereochemistry of the Reaction between Hydrogen Chloride and Rubber.—In the first place, the structure of rubber hydrochloride now established confirms the original assumption that Markownikoff's rule is obeyed in the addition reaction; the chlorine atom adds on to the carbon bearing the methyl side group, and the hydrogen adds on to the $=CH^-$ group. But in addition, it is noteworthy that in the rubber hydrochloride molecule, successive $^-(CH_2)_3{-}CMeCl^-$ groups are alternately left- and right-handed. (The enantiomorphic character ot the group does not depend on the geometry of the chain; it is not possible, by rotating round single bonds, to convert a left- into a right-handed unit.) The precise geometry of the addition reaction depends on the form of the rubber molecule in solution, *i.e.*, whether it is extended or coiled up. If it is extended in solution it may be represented thus :



[Actually the molecule is not planar (Bunn, *loc. cit.*), but the above plane projection is sufficient for the present purpose.] The established structure of rubber hydrochloride implies that if a molecule of hydrogen chloride adds on to double bond *A* on this side of the rubber molecule—above the plane of the paper—then addition to *B* and *C* must also occur on this same side of the rubber molecule; and so on for many units, to give a molecule which is regular for at any rate some hundreds of *A*'s (this being the order of size of the crystals of rubber hydrochloride). If the rubber molecules are coiled up in solution, the geometry of the addition reaction is different, but again some geometrically regular repetition must occur; in other words, it appears that when a hydrogen chloride molecule has added on to one double bond, the atomic grouping so formed has a directing influence on the process of addition to the next double bond.

It is interesting in this connection to note that balata hydrochloride is amorphous (Gehman, Field, and Dinsmore, *loc. cit.*). The balata or gutta-percha hydrocarbon is *trans*-polyisoprene, rubber being the *cis*-form; the amorphous character of balata hydrochloride may mean that, owing to the difference in chain structure, addition of hydrogen chloride does not occur in the geometrically regular way noted in the case of rubber, but in such a way that left- and right-handed groupings are formed indiscriminately, yielding chain molecules which, since they are geometrically irregular in structure, cannot form crystalline arrangements.

Physical Properties of Rubber Hydrochloride.—The mechanical properties of rubber hydrochloride are similar to those of other crystalline polymers : it can be drawn out to several times its length, the crystals becoming oriented in the process, and it remains extended when released. Near the m. p., the extensibility becomes reversible, the material then being more like rubber (Gehman *et al.*, *loc. cit.*); this behaviour is also typical of crystalline polymers. Interest centres on the m. p., which is about 115°, *i.e.*, very much higher than that of rubber (about 0°) and similar to that of polyethylene (115°).

It has been suggested that ease of rotation round the single bonds of long-chain polymer molecules plays a large part in determining the m. p., and that the ease of rotation round the single bonds in any particular molecule is determined by two factors—the bond-orientation energy and the interaction of the atoms or groups held by the bonds. As regards the second factor, we have to imagine, in the case of the rubber hydrochloride molecule, rotation occurring round bond C–$CH_2(2)$ in Fig. 5, and to consider to what extent the rotation of $CH_2(1)$ is hindered by $CH_2(3)$, CH_3, and Cl. [Rotation round bond C–$CH_2(3)$ presents the same geometrical problem.] The hindrance offered by $CH_2(3)$ or by the CH_3 group would be expected to be similar to the hindrance in rubber itself, since the configurations of the moving parts are similar in the two molecules. The hindrance offered by the chlorine atom is expected to be less, since the chlorine atom is a little smaller than a CH_2 or a CH_3 group and also stands further from the carbon atom to which it is attached. Thus, whatever bond rotations occur in the rubber hydrochloride molecule at the m. p., the geometrical hindrance to rotation is not likely to be greater, and may even be less, than in rubber itself. The high m. p. of rubber hydrochloride in comparison with rubber is therefore not to be explained by any steric effects.

Turning to the other factor—the bond-orientation energy—we find that rotation round single bonds is easier when there is an adjacent double bond (as in rubber) than in a saturated molecule (Bunn, *loc. cit.*, 1942). The difference between the m. p.'s of rubber and of its hydrochloride may therefore be due, at any rate partly, to the fact that in rubber every fourth chain bond is a double bond, whereas the hydrochloride molecule is saturated, and the more rigid simply on that account. There are, however, other factors which may also play a part; first, the greater inertia of the moving parts of the rubber hydrochloride molecule owing to the presence of the comparatively heavy chlorine atom, and secondly, the interaction of C–Cl dipoles. Both these factors would tend to increase the m. p. It is not possible at present to assess the relative contributions of these factors.

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136. *Some Alkyl Quinols and Related Compounds.*

By A. H. Cook, I. M. Heilbron, and F. B. Lewis.

The preparation of long-chain acyl quinol diethers is described. These have been reduced to alkyl quinol ethers, which were hydrolysed to alkyl quinols; the last were oxidised to alkyl benzoquinones.

The intermediate acyl quinol ethers were treated with methylmagnesium iodide, olefinic and not *tert.*-alcoholic quinol ethers being obtained; representative *sec.*-alcoholic quinol ethers were prepared by reducing the acyl compounds. The olefinic or alcoholic ethers were also hydrolysed with halogen hydride, but the products were evidently coumarans or chromans. Efforts to synthesise analogues of vitamin E by a similar method were unsuccessful.

Quinols bearing a higher alkyl side chain were required for technical purposes. No success attended attempts to alkylate quinol with *n*-propyl or *tert.*-butyl alcohol in presence of boron trifluoride (cf. Kolka and Vogt, *J. Amer. Chem. Soc.*, **1939**, **61**, 1463; Calcott, Tinker, and Weinmayer, *ibid.*, p. 1010) or with *n*-butyl, amyl, or cetyl alcohol or 1-methyl*cyclo*hexanol in presence of zinc chloride (cf. B.P. 470,852); similar attempts with quinol diethyl ether (Hinton and Nieuwland, *J. Amer. Chem. Soc.*, **1932**, **54**, 2017) were also abandoned. Stearic acid or stearoyl chloride could not be condensed with quinol in presence of zinc chloride (cf. B.P. 287,967); *quinol distearate*, *4-methoxyphenyl palmitate* or *stearate* could not be induced to undergo the Fries reaction.

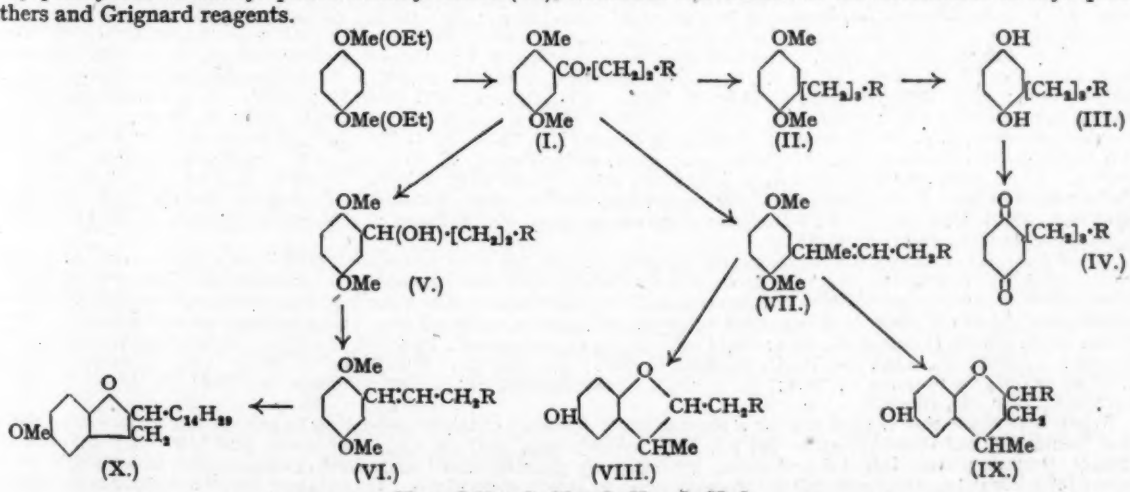
Success in preparing derivatives of acyl quinols was at length achieved by minor modification of the method employed by Cruikshank and Robinson (J., 1938, 2064; cf. also Gulland, *Biochem. J.*, **1932**, **26**, 43) to obtain 2-hydroxy-5-methoxy-*n*-valerophenone. Cruikshank and Robinson allowed quinol dimethyl ether, valeryl chloride, and aluminium chloride to interact at the b. p. of carbon disulphide, whereby removal of one ether group ensued. In the present work, we treated quinol dimethyl ether and quinol diethyl ether with stearoyl, palmitoyl, myristoyl, and lauroyl chlorides in an inert solvent at 0° and in presence of aluminium chloride. In each case an excellent yield of the crystalline *acyl quinol diether* (I) was obtained and only negligible amounts of the monoethers appeared to be formed; this statement is based on the absence of phenolic properties and appreciable active hydrogen content, and quantitative dealkylations; alkyl iodide was only slowly evolved and usually amounted to 85% of that theoretically required (cf. Bateman and Robinson, J., 1941, 402).

The acyl quinol ethers were reduced to *alkyl quinol ethers* (II) in yields of 42—50%; 2 : 5-dimethoxymyristylbenzene was obtained in crystalline form. The action of hydrazine hydrate and sodium methoxide was unsuccessfully attempted and the greatest measure of success in reducing the ketones resulted on applying the original method of Clemmensen; attempts to improve this by adding solvents such as acetic acid or dioxan to the reducing medium resulted in decreased rather than increased yield.

In attempting dealkylation, aluminium chloride in carbon disulphide or hydriodic acid appeared to initiate deep-seated changes and the method finally adopted was to reflux the diethers for a short time with hydrobromic acid.

These crystalline *myristyl-*, *lauryl-*, *palmityl-*, and *stearyl-quinols* (III) were characterised by oxidation with silver oxide to the corresponding *quinones* (IV). The two lower homologues were indefinitely stable, but palmityl- and more particularly stearyl-benzoquinone tended to resinify on crystallisation; this behaviour is shown by some lower alkyl benzoquinones also. Stearylbenzoquinone reacted normally with acetic anhydride to give a colourless triacetoxy-compound, 2 : 4 : 5-*triacetoxystearylbenzene*.

Whilst the difficulties of reducing the above acyl compounds were being overcome, experiments to circumvent this obstacle were begun. 2 : 5-Dimethoxy-stearo- and -palmito-phenone were reduced quantitatively to sec.-*alcohols* (V) by aluminium *iso*propoxide, but, as dehydration of these (with sodium bisulphate) afforded only poor yields of *alkenyl quinol dimethyl ethers* (VI), attention was turned to the interaction of acyl quinol ethers and Grignard reagents.



[R = C_9H_{19}, $C_{11}H_{23}$, $C_{13}H_{27}$, $C_{15}H_{31}$]

2 : 5-Dimethoxy-lauroyl-, -myristoyl-, -palmitoyl-, and -stearoyl-benzene and methylmagnesium iodide furnished not tertiary alcohols but the corresponding *alkenyl quinol dimethyl ethers* (VII), usually obtained at the ordinary temperature as oils. These olefins were demethylated with hydrobromic acid, but the oils were not unsaturated quinols, though the analytical figures were in agreement with such structures. They contained no unsaturated groups and no absorption took place on shaking with platinum in an atmosphere of hydrogen; instead of two hydroxyl groups, only one was present, as was shown by determination of active hydrogen; any possibility of incomplete demethylation could be disregarded on the results of (negative) methoxyl estimations. There can be no doubt, therefore, that these products are to be formulated as *coumarans* or *chromans* (VIII, IX) with structures recalling those of vitamin E. It must be considered probable that their persistence as oils and their reluctance to give crystalline derivatives is due to the co-existence of five- and six-membered oxygen ring structures, and perhaps also to the existence of stereoisomerides. Cyclisation of the olefin from the secondary alcohol obtained by reducing dimethoxypalmitophenone was exceptional; elementary analysis, methoxyl estimations, absence of olefinic linkages and absence of hydroxyl groups all went to confirm that again cyclisation had occurred but with removal of only one methoxyl group; the product is therefore formulated as (X).

(IX; R = $C_{13}H_{27}$) is closely related to vitamin E, from which it differs only in the lack of nuclear and side-chain methyl groups. We were therefore interested to carry out a similar series of reactions starting from ψ-cumoquinol dimethyl ether and palmitoyl chloride. Unfortunately all attempts to prepare the acyl derivative failed. The failure might have been due to "steric hindrance" or to electronic incompatibility occasioned by the presence of nuclear methyl groups. As there seems to be no inhibitory factor in the known syntheses of vitamin E, electronic inhibition seems to be the more acceptable explanation of the difference between quinol and ψ-cumoquinol ethers.

Experimental.

4-Methoxyphenyl Stearate.—Stearoyl chloride (30 g.) and quinol monomethyl ether (11 g.), dissolved in ether (50 c.c.), were treated slowly in the cold with pyridine (20 c.c.). After 2 hours, ether (100 c.c.) was added, and the whole extracted with 10% hydrochloric acid and then with 10% caustic soda solution. The ethereal layer was dried and evaporated; the residual *ester* crystallised from ethanol; yield 25 g., m. p. 50° (Found: C, 76·7; H, 10·8. $C_{25}H_{42}O_3$ requires C, 76·9; H, 10·8%). The *palmitate* was obtained similarly; it crystallised from ethanol, m. p. 51·5° (Found: C, 76·5; H, 10·7. $C_{23}H_{38}O_3$ requires C, 76·3; H, 10·5%).

Acyl Quinol Dimethyl or Diethyl Ethers.—Quinol dimethyl or diethyl ether (1 g.-mol.) in ice-cold tetrachloroethane (500 c.c.) was treated with aluminium chloride (134 g.) with stirring. The fatty acid chloride (C_{12}, C_{14}, C_{16}, C_{18}) (1 g.-mol.) was added slowly, and the whole stirred for a further 12 hrs. The deep red solution was then poured on ice (500 g.), and solvent distilled in steam. The non-volatile ketone was taken up in ether and freed from fatty acid by washing repeatedly with 10% caustic soda solution; it was finally distilled in a vacuum, and the solid product crystallised from methanol.

The following compounds were prepared: 2 : 5-*Dimethoxystearophenone*, m. p. 46°; yield, 60% (Found: C, 77·2; H, 11·0. $C_{26}H_{44}O_3$ requires C, 77·2; H, 10·9%). 2 : 5-*Dimethoxypalmitophenone*, b. p. 205°/0·18 mm., m. p. 51·5°; yield, 69% (Found: C, 76·9; H, 10·7. $C_{24}H_{40}O_3$ requires C, 76·6; H, 10·6%). 2 : 5-*Dimethoxymyristophenone*, b. p. 209°/0·5 mm., m. p. 43°; yield, 62% (Found: C, 75·8; H, 10·4. $C_{22}H_{36}O_3$ requires C, 75·9; H, 10·4%). 2 : 5-*Dimethoxylaurophenone*, b. p. 175—178°/0·2 mm., m. p. 27·5°; yield, 76% (Found: C, 75·3; H, 10·0. $C_{20}H_{32}O_3$ requires C, 75·0; H, 10·0%). 2 : 5-*Diethoxymyristophenone*, b. p. 204°/0·29 mm., m. p. 44·5°; yield, 62% (Found: C, 76·9; H, 10·8. $C_{24}H_{40}O_3$ requires C, 76·6; H, 10·6%). 2 : 5-*Diethoxylaurophenone*, b. p. 180—190°/0·34 mm., m. p. 34—35°; yield, 65% (Found: C, 75·6; H, 10·1. $C_{22}H_{36}O_3$ requires C, 75·8; H, 10·4%). 2 : 4 : 5-*Trimethoxylaurophenone*, m. p. 53°; yield, 60% (Found: C, 72·3; H, 9·7. $C_{21}H_{34}O_4$ requires C, 72·0; H, 9·7%).

The 2 : 4-*dinitrophenylhydrazones* of 2 : 5-diethoxypalmitophenone, 2 : 5-diethoxymyristophenone, and 2 : 5-diethoxylaurophenone were obtained in the normal manner. They formed bright red crystals from ethanol, m. p. 75° (Found: N, 9·9. $C_{32}H_{48}O_8N_4$ requires N, 9·6%), 78° (Found: N, 10·4. $C_{30}H_{44}O_6N_4$ requires N, 10·1%), and 77·5° (Found: N, 10·4. $C_{28}H_{40}O_6N_4$ requires N, 10·6%), respectively.

Alkyl Quinol Ethers.—The acyl quinol ethers (50 g.) were boiled with concentrated hydrochloric acid (250 c.c.) and water (250 c.c.) for 20 hours in presence of amalgamated zinc (100 g.); 50—100 c.c. of concentrated acid were added after 1, 2, and 3 hours. The oil was diluted with ether, the solution washed with aqueous potassium carbonate, and the alkyl quinol ether fractionally distilled. The following were prepared: 2 : 5-*Dimethoxystearylbenzene*, b. p. 188°/0·2 mm.; yield, 42% (Found: C, 80·4; H, 12·0. $C_{26}H_{46}O_2$ requires C, 80·0; H, 11·8%). 2 : 5-*Dimethoxypalmitylbenzene*, b. p. 210°/0·5 mm.; yield, 40% (Found: C, 79·6; H, 11·8. $C_{24}H_{42}O_2$ requires C, 79·6; H, 11·6%). 2 : 5 : *Dimethoxymyristylbenzene*, b. p. 165°/0·5 mm.; yield, 52% (Found: C, 79·1; H, 11·4; $C_{22}H_{38}O_2$ requires C, 79·1; H, 11·4%). 2 : 5-*Dimethoxylaurylbenzene*, b. p. 154°/0·5 mm.; yield, 42% (Found: C, 78·5; H, 11·2. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·1%). 2 : 5-*Diethoxystearylbenzene*, b. p. 201°/0·06 mm.; yield, 48% (Found: C, 80·2; H, 11·9. $C_{28}H_{50}O_2$ requires C, 80·4; H, 12·0%). 2 : 5-*Diethoxypalmitylbenzene*, b. p. 219°/0·1 mm.; yield, 43% (Found: C, 79·7; H, 11·7. $C_{26}H_{46}O_2$ requires C, 80·0; H, 11·8%). 2 : 5-*Diethoxymyristylbenzene*, b. p. 183°/0·1 mm.; yield, 41% (Found: C, 79·5; H, 11·9. $C_{24}H_{42}O_2$ requires C, 79·6; H, 11·6%). 2 : 5-*Diethoxylaurylbenzene*, b. p. 176°/0·7 mm.; yield, 50% (Found: C, 79·1; H, 11·1. $C_{22}H_{38}O_2$ requires C, 79·1; H, 11·3%).

Alkyl Quinols.—Dialkoxyalkylbenzene (40 g.) was refluxed for 4—6 hours with 50% hydrobromic acid (40 g.) and acetic acid (200 c.c.), a further 20 g. of hydrobromic acid being added after 2 hours. The product was allowed to crystallise either directly or after neutralisation with aqueous sodium bicarbonate. The quinols were crystallised from light petroleum without the aid of charcoal, as this caused catalytic oxidation to blue solids. The following were prepared: *Stearylquinol*, m. p. 100·5° (Found: C, 79·5; H, 11·4. $C_{24}H_{42}O_2$ requires C, 79·6; H, 11·6%). *Palmitylquinol*, m. p. 112° (Found: C, 79·1; H, 11·5. $C_{22}H_{38}O_2$ requires C, 79·1; H, 11·4%). *Myristylquinol*, m. p. 110° (Found: C, 78·2; H, 11·3. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·1%). *Laurylquinol*, m. p. 105° (Found: C, 77·6; H, 10·9. $C_{18}H_{30}O_2$ requires C, 77·7; H, 10·8%).

When hydrolysis was carried out for a shorter time, oils were obtained consisting largely of alkylquinol monoether. Thus palmitylquinol dimethyl ether (45 g.), 50% hydrobromic acid (80 c.c.), and acetic acid (100 c.c.), refluxed for 4 hours and then poured into 1·5 l. of water, gave the oily palmitylquinol monomethyl ether, which was distilled (b. p. 200—210°/0·2 mm.) and then crystallised from ethanol; m. p. 47°, yield 15·5 g. It contained 1 active hydrogen atom/mol. (Zerewitinoff determination) and yielded the quinol on further refluxing with hydrobromic acid.

Alkyl Quinones.—The quinol, dissolved in a small amount of ether, was shaken for 2 hours with twice the theoretical amount of silver oxide at room temperature. The filtered solution was evaporated, and the residual quinone recrystallised from ethanol–ether. *Stearylbenzoquinone*, m. p. 76° (Found: C, 80·1, 79·9; H, 11·3, 10·9. $C_{34}H_{40}O_2$ requires C, 80·0; H, 11·1%), *palmitylbenzoquinone*, m. p. 83° (Found: C, 80·0; H, 11·0. $C_{32}H_{36}O_2$ requires C, 79·5; H, 10·8%), *myristylbenzoquinone*, m. p. 77·5° (Found: C, 78·6; H, 10·4. $C_{30}H_{32}O_2$ requires C, 78·9; H, 10·5%), and *laurylbenzoquinone*, m. p. 72° (Found: C, 78·2; H, 10·0. $C_{18}H_{28}O_2$ requires C, 78·3; H, 10·1%), were prepared.

Stearylbenzoquinone (1 g.) dissolved on gentle warming in acetic anhydride (5 c.c.) containing 5 drops of concentrated sulphuric acid. The solution was poured into water, and the precipitated 2 : 4 : 5-*triacetoxystearylbenzene* crystallised from ethanol; it had m. p. 73° (Found: C, 71·4; H, 9·5. $C_{30}H_{46}O_6$ requires C, 71·4; H, 9·5%).

Secondary Alcohols.—Dimethoxypalmitophenone (20 g.), dissolved in a little dry *iso*propyl alcohol, was treated with aluminium *iso*propoxide (5 g.) and the acetone formed was slowly distilled off while dry *iso*propyl alcohol was added at the same rate. On completion (8 hours) the product was poured into dilute hydrochloric acid, and the solid extracted with ether. 1-*Hydroxy*-1-2′ : 5′-*dimethoxyphenylhexadecane* so recovered crystallised from aqueous methanol in colourless leaflets, m. p. 34° (Found: C, 76·3; H, 10·9. $C_{24}H_{42}O_3$ requires C, 76·2; H, 11·1%). It yielded 0·97 mol. of methane with methylmagnesium iodide (Zerewitinoff determination).

The hydroxyhexadecane derivative (12 g.) was heated with anhydrous sodium bisulphate (50 g.) for 3 hours at 200°. The oil was extracted with ether and eventually distilled at 204°/0·015 mm. 1-2′ : 5′-*Dimethoxyphenyl*-Δ^1-*hexadecene* solidified and was crystallised from aqueous ethanol; it had m. p. 43°. It was soluble in the common solvents and was unsaturated towards permanganate, bromine in chloroform, and tetranitromethane (Found: C, 79·7; H, 11·0. $C_{24}H_{40}O_2$ requires C, 80·0; H, 11·1%).

Dimethoxyphenylolefins.—2 : 5-Dimethoxyacylbenzene (40 g.) in dry ether (200 c.c.) was added dropwise to a Grignard reagent prepared from magnesium (2·4 g.), methyl iodide (30 g.), and ether (50 c.c.). The whole was refluxed for 30 mins. and then poured on ice and dilute hydrochloric acid. The ethereal layer was distilled, eventually in a vacuum, to give the olefins; yield, 60—70%. The following were prepared: 1-2′ : 5′-*Dimethoxyphenyl*-1-*methyl*-Δ^1-*octadecene*, b. p. 202°/0·5 mm. (Found: C, 80·5; H, 11·3. $C_{27}H_{46}O_2$ requires C, 80·6; H, 11·5%), 1-2′ : 5′-*dimethoxyphenyl*-1-*methyl*-Δ^1-*hexadecene*, m. p. 35° (from aqueous ethanol) (Found: C, 80·2; H, 11·3. $C_{25}H_{42}O_2$ requires C, 80·2; H, 11·3%), 1-2′ : 5′-*dimethoxyphenyl*-1-*methyl*-Δ^1-*tetradecene*, b. p. 175°/0·2 mm. (Found: C, 79·7; H, 10·9. $C_{23}H_{38}O_2$ requires C, 79·8; H, 11·0%), and 1-2′ : 4′ : 5′-*trimethoxyphenyl*-1-*methyl*-Δ^1-*duodecene*, b. p. 203°/0·5 mm. (Found: C, 75·9; H, 10·4. $C_{23}H_{38}O_3$ requires C, 75·9; H, 10·4%).

Hydroxycoumarans (*Hydroxychromans*).—The dimethoxy-olefins above were demethylated by the same treatment as was used for the dialkoxyalkylbenzenes. The products were repeatedly fractionated in a vacuum; the yields were *ca.* 25% and were reduced on prolonged boiling with hydrobromic acid and acetic acid. The following were prepared: 5-*Methoxycoumaran*-2-*tetradecyl* (6-*methoxy*-2-*tridecylchroman*), b. p. 196°/10·2 mm. (Found: C, 79·4; H, 11·0; OMe, 9·2. $C_{23}H_{38}O_2$ requires C, 79·6; H, 11·0; OMe, 9·0%), 5-*hydroxy*-3-*methyl*-2-*hexadecylcoumaran* (6-*hydroxy*-4-*methyl*-2-*pentadecylchroman*), b. p. 192—194°/0·2 mm. (Found: C, 80·0; H, 10·8. $C_{25}H_{42}O_2$ requires C, 80·2; H, 11·2%), 5-*hydroxy*-3-*methyl*-2-*tetradecylcoumaran* (6-*hydroxy*-4-*methyl*-2-*tridecylchroman*), b. p. 200°/0·2 mm. (Found: C, 79·5; H, 11·0. $C_{23}H_{38}O_2$ requires C, 79·7; H, 11·0%), and 5-*hydroxy*-3-*methyl*-2-*decylcoumaran* (6-*hydroxy*-4-*methyl*-2-*nonylchroman*), b. p. 178—183°/0·2 mm. (Found: C, 78·4; H, 10·3. $C_{19}H_{30}O_2$ requires C, 78·6; H, 10·4%).

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, LONDON, S.W.7. [*Received, July 21st*, 1942.]

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137. *Molecular Volume and Structure. Parts III and IV.*

By T. W. GIBLING.

PART III.

The parachors of carbocyclic compounds are considered; ring corrections and interference corrections due to substitution and interaction of groups containiug carbon, hydrogen, and oxygen are assessed, and group values calculated. Diminutions in the expected parachors of alkylbenzenes and aromatic ethers are attributed to the polarity of the molecules. The parachor of phenyl carbonate agrees with a structure similar to that of the methyl and the ethyl ester. The skew configuration recently suggested for benzil is confirmed by parachor evidence.

THE parachor correction for ring formation may be taken to be the excess of the actual parachor standard value (S.V.) of a simple cyclic compound above the sum of the values of the constituent groups, these being allotted their full values uncorrected for interference. In Part I (J., 1941, 299) it was estimated that the ideal S.V. for (C)·CH_2·(C), uncorrected for interference between the two carbon atoms to which it is attached, is 42·0. Then, for *cyclo*pentane:

S.V., obs.	204·6 (see table, later)
5(C)·CH_2·(C), uncorrected, at 42·0	210·0
*cyclo*Pentane ring correction	−5·4

This correction is really the difference between two quantities: one, greater than 5·4 and of negative sign, representing the diminution in molecular volume caused by the interaction of those carbon atoms which are not linked to each other, and the second, a positive quantity, which measures the increase in volume due to the presence of the ring itself. It follows that in *cyclo*propane, in which all the carbon atoms are linked to each other, the ring correction will be positive. In *cyclo*pentane, with nucleus as inset, there are five equal interference effects, as indicated, and since the angles and distances are approximately those found in an open carbon chain, the total correction for these interferences should be about $-2{\cdot}2 \times 5 = -11{\cdot}0$ (see Part I, *loc. cit.*, p. 302). Hence:

*cyclo*Pentane ring correction, observed	− 5·4
Total internal correction	−11·0
Difference due to presence of ring	+ 5·6

Careful determination, or redetermination, of the parachors of several cyclic paraffins and olefins and of certain of their derivatives has been undertaken by Vogel (J., 1928, 2010; 1938, 1323), and the various corrections adopted here are based mainly upon his most recent results. Thus, ring corrections: *cyclo*pentane, *−5·4*; *cyclo*hexane, *−10·7*. Assuming that no extra correction is required for the fusion of two simple rings (as appears from the parachors of naphthalene and quinoline, recorded later), we may use the following corrections for (*a*) decalin and (*b*) hexahydrohydrindene: (*a*) $-10{\cdot}7 \times 2 = -21{\cdot}4$; (*b*) $-10{\cdot}7 - 5{\cdot}4 = -16{\cdot}1$.

From consideration of the parachors of the simple 5- and 6-carbon *cyclo*-paraffins and olefins and those of their methyl derivatives, it is clear that substitution of CH_3 involves increase in S.V. of *38·8*, the corresponding interference correction being *−3·2* instead of the −4·4 which might have been expected from comparison with open-chain compounds (see Part I, *loc. cit.*). Substitution of CH_2= might be expected to necessitate a similar correction, but for five of the six methylene derivatives of *cyclo*paraffins for which parachors have been determined the correction required seems to be negligible, the increase in S.V. due to substitution of the methylene group being about *31·0*; for methylene*cyclo*hexane, however, the parachor calculated on this basis is 4·5 units above the observed value.

Parachors of cyclic hydrocarbons may be calculated as in the following example, *viz.*, methyl*cyclo*hexane:

5(C)·CH_2·(C), uncorrected, at 42·0	210·0	Σ group values	294·0
$\begin{matrix}(C)\\(C)\end{matrix}\!>$CH·(C), „ „ 28·8	28·8	Ring correction	−10·7
CH_3·(C) „ „ 55·2	55·2	Side-chain correction	− 3·2

Hence S.V., calc., 280·1; add E.C. ("expansion" correction) 0·7; [*P*], calc., 280·8.

(For group values, etc., used here and in other calculations, see p. 666.)

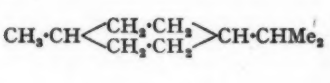
Calculations are often shortened, however, by using normal (corrected) group values for *cyclo*hexyl, etc., which may be obtained as follows:

S.V., methyl*cyclo*hexane	280·1
Deduct CH_3·(C) at 55·2	55·2
S.V., *cyclo*hexyl, C_6H_{11}·(C)	224·9

This is 16·4 units less than S.V., *cyclo*hexane (241·3); hence S.V., *cyclo*hexylene, (C)·C_6H_{10}·(C), = 224·9 − 16·4 = *208·5*; and so on. Correction for interaction of the two substituted groups may have to be applied subsequently.

The corrections required for 1 : 2-, 1 : 3-, and 1 : 4-substitution by carbon atoms appear to be identical with the *o*-, *m*-, and *p*-corrections for aromatic compounds, *viz.*, *o*-(1 : 2), *−2·7*; *m*-(1 : 3), *−1·7*; *p*-(1 : 4), *−2·2* (see xylenes, later). In cyclic paraffins and their derivatives it seems probable that these corrections are inoperative if the substituted groups are in the *trans*-position to each other; Gillespie, Macbeth, and Mills (J., 1940, 280) investigated pairs of geometrical isomerides of the *cyclo*hexane series and, in the three cases in which they were dealing with non-associated *p*-substituted compounds, the parachor of the *trans*-compound was about 2 units greater than that of its *cis*-isomer; the actual differences recorded were as follows: *p*-menthane, 2·2; hexahydrocuminic ester, 1·9; dihydrocryptyl acetate, 1·9.

Calculation of the parachor of *cis-p*-menthane will serve to illustrate the alternative method suggested above:



(C)·C_6H_{10}·(C) at 208·5	208·5	Σ group values	396·3
3(C)·CH_3 „ 55·2	165·6	*p*-correction	−2·2
$\begin{matrix}(C)\\(C)\end{matrix}\!>$CH·(C) „ 22·2	22·2	S.V., calc.	394·1
		E.C. +1·5; [*P*], calc.	395·6

All the determinations in the following table were made by Vogel (J., 1938, *loc. cit.*), except those for 1 : 1-dimethyl*cyclo*hexane (Sugden, J., 1924, **125**, 1177) and the *p*-menthanes (as above). Earlier determinations for several of these hydrocarbons are recorded in Vogel's paper and *Brit. Assoc. Rep.*, 1932, 265.

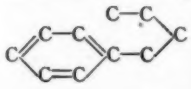
Hydrocarbon.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.	Corrns. applied.
*cyclo*Pentane	204·6	+0·4	205·0	205·0	±0·0	—
Methylene*cyclo*pentane	235·6	+0·5	236·1	235·3	−0·3	—
Methyl*cyclo*pentane	243·4	+0·5	243·9	243·8	−0·0	—
*cyclo*Hexane	241·3	+0·5	241·8	241·8	±0·0	—
Methylene*cyclo*hexane	272·3	+0·7	273·0	268·5	−1·6	—
Methyl*cyclo*hexane	280·1	+0·7	280·8	280·9	+0·0	—
1-Methyl-3-methylene*cyclo*hexane	309·4	+0·9	310·3	311·0	+0·2	−1·7 : *m*-
1-Methyl-4-methylene*cyclo*hexane	308·9	+0·9	309·8	310·1	+0·1	−2·2 : *p*-
1 : 1-Dimethyl*cyclo*hexane	316·7	+1·0	317·7	316·1	−0·5	— *
cis-p-Menthane	394·1	+1·5	395·6	395·6	±0·0	−2·2 : *p*-
trans-p-Menthane	396·3	+1·5	397·8	397·8	±0·0	—
2-Methylene-*trans*hexahydrohydrindene	363·1	+1·3	364·4	364·8	+0·1	−3·4 : 2*m*-
2-Methylene-*trans*decalin	399·3	+1·5	400·8	398·5	−0·6	−3·9 : *m*-, *p*-

* In calculating by the shorter method, note that a correction of −2·2 is required for the grouping C$\begin{matrix}C\\C\end{matrix}\!>$.

The ring correction for benzene, regarded as possessing the Kekulé structure, may be calculated as follows:

S.V., benzene (see table following)	205·6
6(C)·CH=(C), uncorrected, at 36·5 (Part I, *loc. cit.*, p. 303)	219·0
Benzene ring correction	−13·4

In benzene and its homologues both the lengths of the bonds and the angles beteeen them are different from those found in open-chain olefins. The increase in S.V. from benzene to toluene is *39·8*, instead of the 37·6



found when a primary olefin group is converted into a secondary grouping by substitution of CH_3, *i.e.*, the interference correction due to attachment of a carbon atom to the nucleus is *−2·2*, instead of *−4·4*. For the next three members in the series of *n*-alkylbenzenes, the Δ_{CH_2} values appear to be *37·4*, *39·2*, and *38·5*, respectively, after which the normal Δ value of 39·8 is found. It seems that the polarity of the molecule comes into play, causing the side chain to bend backwards towards the ring (see inset)—compare the similar effect supposed to be produced by the carbonyl group (Part II, *loc. cit.*, p. 306). For polyalkylbenzenes, *o*-, *m*-, or *p*-corrections are required, as mentioned before.

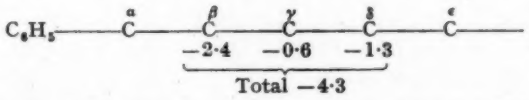
Group values for phenyl, phenylene, etc., may be obtained (as for *cyclo*hexyl, etc., before). Thus:

S.V., toluene	245·4	This is 15·4 less than S.V., benzene; hence S.V., (C)·C_6H_4·(C), *174·8*; S.V., $\begin{matrix}(C)\\(C)\end{matrix}\!\!>\!C_6H_3$·(C), *159·4*.
Deduct CH_3·(C)	55·2	
S.V., phenyl, C_6H_5·(C)	190·2	

(*o*-, *m*-, or *p*-Corrections may have to be applied subsequently.)

The full group values, uncorrected for outside interference, are as follows: C_6H_5·(C), 192·4; (C)·C_6H_4·(C), 179·2; $\begin{matrix}(C)\\(C)\end{matrix}\!\!>\!C_6H_3$·(C), 166·0.

If the normal group values are used (see p. 666), the corrections to be applied in an aromatic side chain will be as follows:



These corrections for the β, γ, and δ carbon atoms are the differences between the Δ values recorded above (37·4, 39·2, 38·5) and the normal Δ value (39·8). Aromatic side-chain corrections, like carbonyl corrections, apply to only one branch in a divided chain.

All the experimental values quoted in the following table are taken from the British Association list (*loc. cit.*).

Aromatic hydrocarbon.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs. (mean).*	Diff., %.	Corrections applied.
Benzene	205·6	+0·4	206·0	206·0[4]	±0·0	—
Toluene	245·4	+0·6	246·0	246·0[5]	±0·0	—
Ethyl-benzene	282·8	+0·8	283·6	283·6[3]	±0·0	−2·4 : Ar.† β
Propyl- ,,	322·0	+1·0	323·0	322·6[2]	−0·1	−3·0 : Ar. β, γ
Butyl- ,,	360·5	+1·3	361·8	361·7	−0·0	−4·3 : Ar. β, γ, δ
Amyl- ,,	400·3	+1·6	401·9	402·0	+0·0	,, ,,
Hexyl- ,,	440·1	+1·9	442·0	442·0	±0·0	,, ,,
o-Xylene	282·5	+0·8	283·3	283·3[2]	±0·0	−2·7 : *o*-
m- ,,	283·5	+0·8	284·3	284·3[5]	±0·0	−1·7 : *m*-
p- ,,	283·0	+0·8	283·8	283·8[3]	±0·0	−2·2 : *p*-
Mesitylene	319·9	+1·0	320·9	320·7[2]	−0·1	−5·1 : 3*m*-
p-Ethyltoluene	320·4	+1·0	321·4	321·7	+0·1	−4·6 : Ar. β; *p*-
p-Cymene	358·0	+1·2	359·2	358·8	−0·1	,, ,,
Naphthalene	311·8	+0·9	312·7	312·5	−0·1	—

* The figures in brackets show the numbers of independent observations upon which the means are based.
† Aromatic side-chain correction (see above).

The parachor of naphthalene agrees very closely with that calculated on the assumption that no appreciable interference effects are involved apart from those produced in ring formation. This assumption is confirmed by the parachors of other substances containing two simple fused-ring systems, *e.g.*, decalin and hexahydrohydrindene and derivatives (see elsewhere in this part), and also by comparison of the parachors of quinoline and pyridine with those of naphthalene and benzene:

	[*P*], obs.	E.C.	S.V., obs.		S.V., calc. (as above).
Quinoline	306·4	−0·9	305·5	Naphthalene	311·8
Pyridine	199·8	−0·5	199·3	Benzene	205·6
Difference			106·2		106·2

For cyclic ketones we have to consider the parachor value of the group (C)·CO·(C). The normal S.V., 50·9, derived from the parachor of acetone (Part II, *loc. cit.*, p. 307) includes two sets of interferences: (*a*) that between two methyl groups attached to a common carbon atom, (*b*) those between each of the methyl groups and the

oxygen atom. The correction for (*a*) may be taken to be −2·2. In cyclic ketones, interference between the oxygen atom and the atoms constituting the ring is not likely to extend beyond those carbon atoms which are linked to the carbon of the carbonyl group, and therefore, when the ring angle does not differ greatly from the angle formed by the three carbon atoms in acetone, the reduction in parachor produced by the interference effects (*b*) may be taken to be substantially unchanged in such ring compounds. Hence, the partially corrected value of 53·1 (50·9 + 2·2) may be used for (C)·CO·(C) here. Parachors so calculated agree reasonably well with the experimental values, especially for cyclic ketones containing a six-carbon ring. The method of calculation is shown for *p*-benzoquinone :

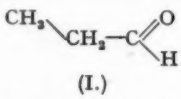
4(C)·CH=(C), uncorr. at 36·5	146·0	Ring corrn. (as benzene)	−13·4
2(C)·CO·(C), part. corr. at 53·1	106·2	*p*- „ (as *p*-xylene)	− 2·2
Σ group values	252·2	Hence S.V. = ...	236·6

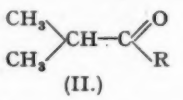
In the following table, observed values are each the mean of several concordant determinations made at different temperatures—the last two (quinones) by Sugden (J., 1927, 2880), the remainder by Vogel (1938, *loc. cit.*), who also records previous determinations for all the monoketones except *trans*-hexahydro-β-hydrindone.

Cyclic ketone.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.	Corrns.* applied.
*cyclo*Pentanone	215·7	+0·4	216·1	214·1	−0·9	—
3-Methyl*cyclo*pentanone	252·8	+0·6	253·4	251·6	−0·8	−1·7 : *m*-
*cyclo*Hexanone	252·4	+0·6	253·0	252·2	−0·3	—
2-Methyl*cyclo*hexanone	288·5	+0·8	289·3	289·1	−0·1	−2·7 : *o*-
3- „	289·5	+0·8	290·3	290·3	±0·0	−1·7 : *m*-
4- „	289·0	+0·8	289·8	289·8	±0·0	−2·2 : *p*-
trans-Hexahydro-β-hydrindone	343·2	+1·1	344·3	344·5	+0·1	−3·4 : 2*m*-
trans-β-Decalone	379·4	+1·4	380·8	382·1	+0·3	−3·9 : *m*-, *p*-
p-Benzoquinone	236·6	+0·5	237·1	236·8	−0·1	−2·2 : *p*-
Toluquinone	272·0	+0·7	272·7	272·0	−0·3	−6·6 : *o*-, *m*-, *p*-

* *o*-, *m*-, and *p*-Corrections are taken to be the same as those found for the xylenes.

The interference effect due to attachment of a carbonyl group, −CO·R, to the benzene ring appears to be about the same as that found in the corresponding open-chain grouping, as in (I) or (II); *i.e.*, the correction may be taken as −2·0 (see Part II, *loc. cit.*, p. 305).


(I.)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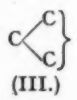
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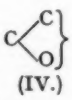
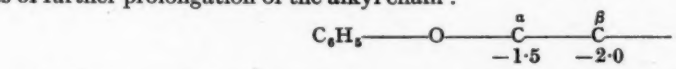

(IV.)

(V.)

Carbonyl compound.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.	Corrns. applied.
Benzaldehyde	255·5	+0·6	256·1	255·1*[3]	−0·4	−2·0 : carb. β
Acetophenone	291·9	+0·8	292·7	293·1†[2]	+0·1	−4·4 : carb. β; Ar. β
Methyl benzoate	309·8	+0·9	310·7	310·4	−0·1	−2·0 : carb. β
Ethyl phthalate	490·1	+2·4	492·5	491·0‡[2]	−0·3	−6·7 : 2 carb β; *o*-

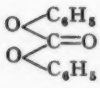
* Mean of 254·0, 255·1, 256·2.
† Sugden (J., 1924, **125**, 1177), 293·8; Hammick and Andrew (J., 1929, 754), 292·4.
‡ Beck, Macbeth, and Pennycuick (J., 1932, 2258), 490·0; Bowden and Butler (J., 1939, 77), 492·0. The other references are given in the British Association list (*loc. cit.*).

Interferences between the nucleus and the oxygen side chains of aromatic ethers are likely to resemble those found in alkylbenzenes. Since substitution in the benzene ring by a carbon atom involves the same correction, −2·2, as the grouping (III), it is probable that for substitution of an oxygen atom a correction of ***−2·6*** will be required, *i.e.*, the same as for the grouping (IV). If this is correct, S.V., C_6H_5·(O) will be ***189·8*** [cf. S.V., C_6H_5·(C), 190·2]. From the parachors of anisole and its derivatives it appears that interference between the ring and the methyl group necessitates a correction of ***−1·5***, while the mean parachor value, 303·3[3], observed for phenetole suggests that for the next carbon atom the extra correction is ***−2·0***. No data are available to show the effects of further prolongation of the alkyl chain :



Aromatic ether.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.	Corrns. applied.
Anisole	265·0	+0·6	265·6	265·5[4]	−0·0	−1·5 : Ar·O*α
o-Methoxybenzaldehyde ...	312·2	+0·9	313·1	312·4[2]	−0·2	−6·7 : Ar·O*α; carb. β; *o*-
p- „ „ ...	312·7	+0·9	313·6	313·9	+0·1	−6·2 : Ar·O*α; carb. β; *p*-

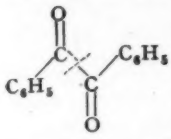
* Aromatic oxygen side chain correction (as above).



Phenyl carbonate may be presumed to have the structure inset (see alkyl carbonates, Part II, *loc. cit.*), in which case no extra interference is to be expected, either between the doubly-linked oxygen atom and the rings, or between the rings themselves. Then,

$2C_6H_5$·(O) at 189·8	379·6	Add E.C. 2·1; then [*P*], calc., 467·2; [*P*], obs., 467·4; Diff. %, +0·0
$O{=}C[O(C)]_2$ at 85·5	85·5	
S.V., calc.	465·1	

For aromatic and other cyclic compounds of more complicated type, as for other substances containing two or more groups with comparatively large polar or steric effects, estimation of the interference corrections required is often difficult, because the exact spatial relationships of the various groups are seldom determinable with certainty. Consideration of such compounds is better postponed until more data have been accumulated. The parachor of benzil, however, confirms the most recent views regarding its structure. If the two halves of the molecule (as inset) lie in the same plane, as was formerly suggested, a considerable amount of interference is to be expected; but the total correction, as derived from the parachor determined, is only −3·6. Caldwell and Le Fèvre (*Nature*, **1939**, **143**, 803; J., 1614), from dipole-moment measurement of benzil in solution, and Knaggs and Lonsdale (*Nature*, *ibid.*, p. 1023), from *X*-ray measurements of the crystals, conclude that the molecule has a skew configuration in which the two benzoyl units lie in planes approximately at right angles to each other. If this is also the configuration in the pure liquid, then the extra interference in each half of the molecule will be the same as in benzaldehyde, *i.e.*, that between the carbonyl group and the ring to which it is attached. Adopting the skew configuration for benzil and its derivatives, one obtains the following results:

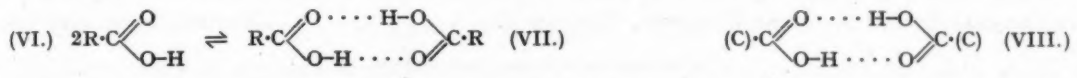


Compound.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.	Corrns. applied.
Benzil	478·2	+2·2	480·4	480·8	+0·1	−4·0 : 2 carb. *β*
2 : 2′-Dimethoxybenzil	591·6	+3·5	595·1	596·8	+0·3	−12·4 : 2 carb. *β*; 2*o*-; 2Ar·O*α*

Part IV.

The parachors of the normal fatty acids show that their molecules are mainly in the dimeric form at ordinary temperatures. A value for the parachor of dimeric acetic acid is determined by extrapolation to absolute zero of the parachors recorded at various temperatures. Values are calculated for the parachors of the dimers of carboxy-acids, and these are compared with the experimental values.

Determination of the mean standard values (S.V.) of the parachors of the normal fatty acids—derived, as explained in Part I (J., 1941, 299), from the observations recorded in *Brit. Assoc. Rep.*, 1932, 265—shows that, among the earlier members in the series, the Δ_{CH_2} value (*i.e.*, the increase in S.V. produced by addition of CH_2 to the structure) varies in much the same way as it does among the corresponding alkyl esters (Part II, J., 1941, 306). Thus, the average value of 38·3 (*i.e.*, 1·5 units less than the normal 39·8) between the second and the fifth member in the series agrees exactly with the results found for the corresponding esters, and is to be explained presumably by interference between the atoms of the carbonyl group and the neighbouring atoms in the attached carbon chain. From the fifth member onwards, however, as far as the eighteenth, the mean Δ value is 40·85, which is more than a whole unit *greater* than the normal value for Δ_{CH_2}, as found in the paraffins. Deviations from this normal value found among the members of the other classes of compounds already considered have been on the negative side and have been attributed to interference between atoms in the same molecule. Many of the physical properties of carboxy-acids show that in the liquid condition their molecules are associated. The association continues into the vapour state and is dependent upon the formation of a dimeric modification (VII) which exists in equilibrium with the monomeric form (VI), the proportion of the two



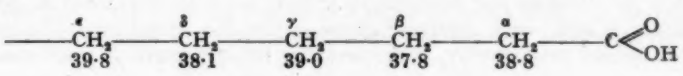
(VI.) (VII.) (VIII.)

kinds of molecule varying with the temperature. Obviously, the anomalous values of Δ_{CH_2} found among the higher fatty acids are due to the fact that, at the temperatures of parachor determination, these acids exist mainly in the dimeric form. Their parachors then lie, not between 365 and 778, as recorded, but between 730 and 1556, for which values of the parachor the difference for adjacent members in the series increases from twice 40·4 to twice 41·1 (see Part I, *loc. cit.*, Conversion Table, p. 304).

The parachor of acetic acid (as $C_2H_4O_2$) has been determined at a series of temperatures from 10° to 280° (Sugden, J., **1924**, **125**, 37; "The Parachor and Valency," **1930**, 167). A graph of [*P*] against *T* yields a curve which clearly represents the dissociation of the dimeric form into single molecules, and extrapolation to zero temperature gives [*P*] = 130·2. Thus, the parachor for the dimer appears to be 260·4, and since the "expansion correction" (E.C.) for this number is −0·6 (see Part I, *loc. cit.*), the "standard value" (S.V.) is 259·8.

Then,	S.V., dimeric acetic acid (VII; R = CH_3)	259·8
	Deduct $2CH_2$– at 55·2	110·4
	S.V., $(CO{\cdot}OH)_2$ nucleus (VIII)	149·4

Assuming that the values for Δ_{CH_2} are the same as those for the corresponding esters (as the parachors of the earlier fatty acids indicate), one must use the following increments for replacement of H– by CH_2– at the points indicated in a carbon chain:



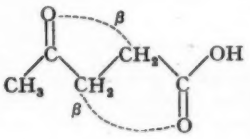
or, taking the standard value for the $(CO{\cdot}OH)_2$ nucleus (VIII) to be 149·4 as above, one may allot to each alkyl group in the chain its normal value and then apply the following "carbonyl corrections" (which, in the case of a divided chain, refer to only one branch): β, −2·0; γ, −0·8; δ, −1·7: total for the three, −4·5 (see Part II, *loc. cit.*).

From the parachors determined by Hunten and Maass (*J. Amer. Chem. Soc.*, 1929, **51**, 153) for seven of the members between octoic and stearic acid, inclusive, it appears that, under experimental conditions, practically all the molecules of these substances were in the dimeric state. Two full "carbonyl corrections" of −4·5 have been applied to each of the calculated standard values in the following table.

Normal Fatty Acid Dimers, $(C_nH_{2n}O_2)_2$.

n.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.	*n*.	S.V., calc.	E.C.	[*P*], calc.	[*P*], obs.	Diff., %.
8	728·4	+ 5·3	733·7	731·2	−0·3	16	1365·2	+19·2	1384·4	1386·4	+0·1
10	887·6	+ 8·0	895·6	895·4	−0·0	17	1444·8	+21·5	1466·3	1466·4	+0·0
12	1046·8	+11·2	1058·0	1065·6	+0·7	18	1524·4	+24·0	1548·4	1556·4	+0·5
14	1206·0	+14·9	1220·9	1211·6	−0·8						

The reasonably good agreement of calculated and experimental parachors in the above table affords confirmation of the approximate accuracy of the parachor of dimeric acetic acid obtained by extrapolation, and also further confirmation of the accuracy of the correction used to counteract the "expansion effect" (see Part I, *loc. cit.*).



The parachors of undecylenic acid and lævulic acid (Mumford and Phillips, J., 1929, 2112) indicate that the molecules of these acids were also mainly in the dimeric form. For the former, two full carbonyl corrections of −4·5 are needed, as in the higher fatty acids above; for the latter, two carbonyl β corrections (−2·0 each) appear to be required for each half of the single molecule, which suggests that the configuration is planar (see inset).

Acid (dimer).	S.V., calc.	E.C.	*P*, calc.	*P*, obs.	Diff., %.
Undecylenic	945·2	+9·1	954·3	956·4	+0·2
Lævulic	512·8	+2·6	515·4	517·2	+0·3

Normal group values, determined in Parts I and II (J., 1941, 299), which have been used for calculations in Parts III and IV, are as follows:

$CH_3{\cdot}(C)$, 55·2; $(C){\cdot}CH_2{\cdot}(C)$, 39·8; $\begin{matrix}(C)\\(C)\end{matrix}\!\!>\!CH{\cdot}(C)$, 22·2; $\begin{matrix}(C)\\(C)\end{matrix}\!\!>\!C\!<\!\begin{matrix}(C)\\(C)\end{matrix}$, 2·4. (Values uncorrected for mutual interference between the attached carbon atoms are 55·2, 42·0, 28·8, and 15·6, respectively.) $CH_2{=}(C)$, 49·7; $(C){\cdot}CH{=}(C)$, 34·3; $\begin{matrix}(C)\\(C)\end{matrix}\!\!>\!C{=}(C)$, 16·7. (Uncorrected values: 49·7, 36·5, and 23·3, respectively.) $(C){\cdot}O{\cdot}(C)$, 21·5; $(C){\cdot}CHO$, 67·3; $(C){\cdot}CO{\cdot}(C)$, 50·9; $(C){\cdot}CO{\cdot}O{\cdot}(C)$, 66·4; $O{=}C[O(C)]_2$, 85·5. Interference corrections for simple groupings are as follows: $C\!<\!\begin{matrix}C\\C\end{matrix}\Big\}$ and $C\!<\!\begin{matrix}C\\C\end{matrix}\Big\}$ −2·2; $C\!<\!\begin{matrix}C\\O\end{matrix}\Big\}$, −2·6.

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138. *Tetra-aryl-phosphonium, -arsonium and -stibonium Salts. Part II. The Mechanism of their Formation by the Aluminium Chloride Reaction.*

By DONALD R. LYON and FREDERICK G. MANN.

The tetraphenylarsonium ion can be formed by the following reactions: (*a*) Triphenylarsine with aluminium chloride gives an addition product $[Ph_3As{\rightarrow}AlCl_3]$ which is thermally stable to *ca.* 250°, but reacts readily with bromobenzene at *ca.* 200° to give the above ion. (*b*) Diphenylchloroarsine gives a product $[Ph_2ClAs{\rightarrow}AlCl_3]$ which conversely undergoes thermal decomposition when heated alone at 200° to give the arsonium ion and arsenic, but does not yield the ion with boiling bromobenzene. (*c*) Phenyldichloroarsine gives a product $[(PhCl_2As)_3AlCl_3]$ in which the arsine on heating undergoes disproportionation to $AsCl_3$ and $AsPh_2Cl$, the latter then reacting as in (*b*). (*d*) A mixture of benzene and arsenic chloride in the presence of aluminium chloride gives phenyldichloroarsine, which then reacts as in (*c*).

Tetra-*o*-tolyl-phosphonium and -arsonium compounds could not be prepared: the isomeric *m*- and *p*-compounds were obtained without difficulty.

IN Part I (J., 1940, 1192) Chatt and Mann showed that tetraphenylarsonium salts, $AsPh_4X$, were formed when aluminium chloride was heated with (*a*) triphenylarsine, (*b*) diphenylchloroarsine, (*c*) phenyldichloroarsine, (*d*) a mixture of benzene and arsenic trichloride: the yield of the arsonium salt in (*a*) was increased if the arsine was previously mixed with moderate, and decreased if mixed with excessive, quantities of bromobenzene. In the reaction (*b*), benzene and elementary arsenic were also detected as products. Tetraphenylphosphonium and -stibonium salts were similarly prepared by the interaction of aluminium chloride with triphenyl-phosphine and -stibine respectively, bromobenzene being present in each case.

This initial exploratory work was performed with stock " resublimed " aluminium chloride which had not been specially purified. The mechanism of the above reactions, which have now been studied in detail with reagents of known purity, will be considered in turn.

(a) *Triphenylarsine.* This arsine combines readily with pure aluminium chloride to give the crystalline addition product *trichlorotriphenylarsinealuminium*, $[Ph_3As\rightarrow AlCl_3]$, a compound of 4-covalent aluminium similar in type to the well-known compounds $[H_3N\rightarrow AlCl_3]$ and $[C_5H_5N\rightarrow AlCl_3]$ (cf. Klemm, Clausen, and Jacobi, *Z. anorg. Chem.*, 1931, **200**, 343, 367; Plotnikov and Valjasny, *J. Gen. Chem. Russ.*, 1931, **1**, 823). This addition product, although chemically very reactive, is thermally stable in an inert atmosphere and can be heated to *ca.* 250° without change, and therefore does not give the arsonium salt when heated alone below this temperature. Its chemical reactivity * is shown by two reactions: (i) When a current of air at room temperature is passed through a suspension of the addition product in benzene, bromobenzene, or tetralin, smooth oxidation to triphenylarsine oxide occurs; triphenylarsine alone is not oxidised in these circumstances. (ii) When a mixture of the addition product and bromobenzene (1 mol.) is heated at 200° for 2 hours, a ready reaction occurs with production of the tetraphenylarsonium salt, no by-products being detected. There is little doubt, therefore, that this reaction consists in the direct union of the reactants,

$$[Ph_3As\rightarrow AlCl_3] + PhBr = [Ph_4As][AlCl_3Br] \longrightarrow Ph_4AsI \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and that the complex salt so formed, when subsequently extracted with hot water and treated with potassium iodide, thus gives the arsonium iodide. That the bromobenzene is a reagent, and is not acting solely as a solvent or flux, is shown by the facts that (1) no elementary arsenic is liberated, although conversion of the tertiary arsine addition product alone into the arsonium salt would probably necessitate arsenic formation and (2) the use of other aryl halides gives mixed arsonium salts. For instance, in the presence of aluminium chloride, triphenylarsine reacted with *p*-bromotoluene, and diphenyl-*p*-tolylarsine with bromobenzene, to give in each case the triphenyl-*p*-tolylarsonium ion, which was isolated as the *iodide* and the *thiocyanate*; diphenyl-*p*-tolylarsine similarly reacted with *p*-bromotoluene to give ultimately *diphenyldi*-p-*tolylarsonium iodide*, and tri-*p*-tolylarsine reacted with bromobenzene to give *phenyltri*-p-*tolylarsonium iodide*. The formation of compounds of type $[Ph_4As][AlCl_3Br]$ in these reactions is not unexpected: these are closely similar to compounds of type $R[AlCl_4]$ which are now known beyond reasonable doubt to occur in the Friedel–Crafts reaction (Wohl and Wertyporoch, *Ber.*, 1931, **64**, 1357, 1369; Fairbrother, *Trans. Faraday Soc.*, 1941, **37**, 763) and demonstrate the readiness of aluminium chloride to pass into a complex $[AlX_4]$ anion.

The initial ready formation of the addition compound $[Ph_3As\rightarrow AlCl_3]$ and the fact that the reactions described under (i) and (ii) above will occur with either this compound or an equimolecular mixture of the tertiary arsine and aluminium chloride, but not in the absence of the chloride, prove that this compound is the essential reactive intermediate in the tertiary arsine reactions.

When, however, the pure resublimed aluminium chloride was exposed to the air in a shallow layer for 15 minutes, and then mixed with triphenylarsine and heated in the absence of bromobenzene, benzene was evolved from 120°, and the product then contained much tetraphenylarsonium salt. This marked difference attending the use of slightly hydrolysed aluminium chloride is undoubtedly due to the latter evolving hydrogen chloride, which then attacks the triphenylarsine giving benzene and diphenylchloroarsine; the latter then reacts directly with aluminium chloride to give the tetraphenylarsonium salt as described below (see b).

$$Ph_3As + HCl = Ph_2AsCl + C_6H_6$$

It is noteworthy that, although Blicke and Monroe (*J. Amer. Chem. Soc.*, 1935, **57**, 720) have shown that triphenylarsine oxide treated with phenylmagnesium bromide gives the tetraphenylarsonium ion, the arsine oxide cannot be an intermediate in the reactions we have studied, since, when heated with aluminium chloride and bromobenzene under many varied conditions, it always gave ultimately after the usual extraction only triphenylarsine hydroxy-salts.

(b) *Diphenylchloroarsine.* The mechanism of the formation of the arsonium salts from this arsine is entirely different from that from the tertiary arsine. Diphenylchloroarsine similarly combines with pure aluminium chloride to give *trichlorodiphenylchloroarsinealuminium*, $[Ph_2ClAs\rightarrow AlCl_3]$, which we have isolated only as a viscous syrup. It is, however, very reactive, and even a few seconds' exposure to the air causes formation of a solid surface film. When the addition product is refluxed with bromobenzene no tetraphenylarsonium ion is formed. When, however, the addition product alone is heated to 200°, decomposition occurs readily with the formation of the arsonium ion and of much elementary arsenic. This would appear to be initially a direct thermal decomposition (2): the fate of the chlorine formed is uncertain, but since Blicke and Monroe

$$2[Ph_2ClAs\rightarrow AlCl_3] = [Ph_4As]Cl + 2AlCl_3 + As + Cl \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(*loc. cit.*) have shown that the arsonium ion readily forms stable trihalides of type $[PH_4As]X_3$, it is probable that the excess chlorine is absorbed to give $[Ph_4As]Cl_3$. The latter would be largely decomposed on extraction with boiling water, but it is significant that only in these experiments did the subsequent precipitation with

* This great reactivity seems to be associated with the co-ordinate link; *e.g.*, Harley-Mason and Mann have shown that triphenylphosphine sulphide, $Ph_3P\rightarrow S$, when heated with excess of methyl iodide at 100° gives an almost theoretical yield of tetramethylphosphonium iodide, whereas triphenylphosphine similarly treated gives solely triphenylphosphine methiodide (unpublished work).

potassium iodide give arsonium iodide coloured yellow by traces of tri-iodide. No evidence that the chlorine combined with the arsenic to form arsenic trichloride could be obtained.

The above thermal decomposition of the pure addition product, or of an equimolecular mixture of the monochloroarsine and pure aluminium chloride, produces no benzene. When, however, a partly hydrolysed sample of aluminium chloride is used, benzene is freely evolved and the yield of the arsonium ion falls markedly. The explanation, as before, is that the hydrogen chloride produced on heating converts the monochloroarsine into phenyldichloroarsine and benzene; the high yield of benzene from a much hydrolysed sample indicates that this degradation may even proceed down to arsenic trichloride itself.

(c) *Phenyldichloroarsine.* A third mechanism occurs here. This arsine, even in the presence of an excess of aluminium chloride, gives *trichlorotris(phenyldichloroarsine)aluminium* * $[(PhCl_2As)_3AlCl_3]$, a non-ionic compound containing 6-covalent aluminium, as in the well-known compounds $[Al(H_2O)_6]Cl_3$ and $K_3[Al(C_2O_4)_3]$. This addition product, which has also been obtained only as a viscous but very reactive syrup, gives rise on heating to the arsonium ion, arsenic trichloride, and elementary arsenic. It follows that the essential reaction is the familiar disproportionation under the influence of the aluminium chloride (3, *a*), and that the diphenyl-

$$(a)\ 4PhCl_2\overset{*}{A}s = 2AsCl_3 + 2Ph_2AsCl \quad (b)\ 2Ph_2AsCl = Ph_4AsCl + As + Cl \quad . \quad . \quad . \quad . \quad . \quad (3)$$

chloroarsine thus produced then gives the arsonium ion and arsenic as discussed above (3, *b*). In these two equations, the co-ordinated aluminium chloride is omitted for simplicity. This mechanism is confirmed by the facts that (i) the arsenic trichloride was isolated, (ii) the elementary arsenic deposited was 21% (theoretical value, 25%) of that present in the original dichloroarsine.

The use of partly hydrolysed aluminium chloride again furnished benzene by the usual mechanism.

(d) *Benzene and arsenic trichloride.* A mixture of these compounds when heated with aluminium chloride is known to give phenyldichloroarsine, and then (in small quantity) diphenylchloroarsine. The reaction of the latter to give the arsonium ion will then, of course, be as under (b) above.

It follows from the foregoing work that the arsonium ion can arise in only two ways: by the interaction of $[Ph_3As\rightarrow AlCl_3]$ and bromobenzene, and by the thermal decomposition of $[Ph_2ClAs\rightarrow AlCl_3]$.

The mechanism of the formation of the tetraphenylphosphonium ion has not been investigated in detail. It is significant, however, that triphenylphosphine when mixed with aluminium chloride undergoes spontaneous oxidation at room temperature to triphenylphosphine oxide, although the pure phosphine alone is quite stable; this behaviour is strictly analogous to that of the arsine and is almost certainly due to the formation of an addition product $[Ph_3P\rightarrow AlCl_3]$.

The influence of substituents in the benzene ring upon the ease of formation of the tetra-arylarsonium ion has been briefly investigated. Theoretical considerations would indicate that a highly stable tetra-*o*-tolylarsonium ion should be readily formed, because the electromeric effect of the four *o*-methyl groups would cause strong electron pressure on the $\overset{+}{A}s$ atom and so stabilise the ion. In the *p*-tolyl series, the effect of the *p*-methyl groups should be similar but weaker owing to their greater distance from the $\overset{+}{A}s$ atom, whereas the tetra-*m*-tolylarsonium ion, in which the electromeric effect is reversed, should be less stable and less easily prepared than the unsubstituted ion. All attempts, over a wide variety of conditions, to prepare tetra-*o*-tolylarsonium salts failed, however; in all cases oxidation occurred, and the usual hot aqueous extraction of the product, followed by precipitation with sodium bromide, gave the *tri-o-tolylarsine hydroxy-oxybromide* (I) or the *oxydibromide* (II) according to the conditions employed. This failure to prepare the ion must presum-

(I.) $(o\text{-}C_6H_4Me)_3As(OH)\rangle O\langle(o\text{-}C_6H_4Me)_3AsBr$ $\qquad$ (II.) $(o\text{-}C_6H_4Me)_3As(Br)\rangle O\langle(o\text{-}C_6H_4Me)_3AsBr$

ably be due to the powerful steric effect of the four *o*-methyl groups. The tetra-*p*-tolylarsonium ion was readily formed in accordance with theory, whereas the formation of the tetra-*m*-tolylarsonium ion was not noticeably more difficult than that of the tetraphenylarsonium ion itself. Similar results were obtained with the phosphorus analogues: tetra-*o*-tolylphosphonium salts could not be prepared, the *tetra*-p-*tolyl* salts were readily formed, and the *tetra*-m-*tolyl* salts were prepared under similar conditions to the phenyl salts themselves.

The tetra-arylarsonium ions prepared in this work could usually be precipitated as their highly crystalline, slightly soluble thiocyanates; these frequently formed hydrates, an abnormal property of thiocyanates.

In view of the insecticidal value of triphenylbenzyl- and other quaternary phosphonium salts (D.R.P. 528,704; B.P. 312,163; U.S.P. 1,921,364) and the known toxic action of certain alkyl thiocyanates on lice, the action of tetraphenyl-phosphonium and -arsonium thiocyanates and other salts on lice has been investigated by Prof. P. A. Buxton and Dr. J. R. Busvine at the London School of Hygiene and Tropical Medicine, but the toxic action was too mild to be useful.

Experimental.

The names of solvents used for recrystallisation are given in parenthesis immediately after the names of the compounds concerned. "Pure" aluminium chloride referred to below was always material which had been freshly sub-

* Hunt and Turner (J., 1925, **127**, 998) have described a crystalline addition compound, $PhCl_2As,AlCl_3$. Their analytical value (Al, 38·3%) indicates, however, an error in the identification of this compound, which actually requires Al, 7·6%.

limed in an atmosphere of hydrogen chloride and then stored in a vacuum until required; "impure" material refers to this pure material which had been exposed to air and partly hydrolysed as described on p. 667.

(A) *Trichlorotriphenylarsinealuminium.*—Pure powdered aluminium chloride (2·25 g.) was added to a solution of triphenylarsine (5 g., 1 mol.) in pure carbon disulphide (50 c.c.). On vigorous shaking, the chloride largely dissolved and a fine white sludge separated and rapidly solidified. The clear supernatant solution was quickly decanted and concentrated in a vacuum at room temperature. The colourless crystals of the above *addition product* which separated were rapidly collected with minimum exposure to the air, and dried in a vacuum (Found: C, 45·8; H, 3·8; Cl, 24·2; Al, 6·3. $C_{18}H_{15}Cl_3AlAs$ requires C, 49·1; H, 3·4; Cl, 24·2; Al, 6·1%. Low and inconsistent carbon values were always obtained). The solidified sludge was an impure sample of this material and gave many of its reactions.

(a) *Oxidation to triphenylarsine oxide.* Dry air was passed through a mixture of powdered triphenylarsine (2 g.) and pure aluminium chloride (0·9 g., 1 mol.) in bromobenzene (15 g.) at room temperature for 15 hours. The product, when extracted with hot water (100 c.c.), filtered, and treated with potassium iodide (10 g.) and acetic acid, gave triphenylarsine hydroxy-iodide (1·2 g.), m. p. 161—164° (mixed and unmixed); this iodide when treated with picric acid gave the hydroxy-picrate, m. p. 168—169° (mixed and unmixed), and when boiled with water gave the crystalline dihydroxide, which melted at 118°, resolidified, and remelted at 193—195° [Michaelis (*Annalen*, 1902, **321**, 164) gives $Ph_2As(OH)_3$, m. p. 116° and Ph_3AsO, m. p. 189°]. This experiment was repeated successfully by using benzene or tetralin in place of the bromobenzene; the omission of the aluminium chloride, or replacement of the air by hydrogen, caused the arsine to remain unchanged. When the above mixture (using, however, 7·5 g. bromobenzene) was kept for 24 hours in a flask open to the air through a calcium chloride tube, and then heated at 180° for 1 hour, the hydroxy-iodide was again obtained. Repetition of these experiments with the pure addition product, $[Ph_3As\rightarrow AlCl_3]$, instead of the mixture of arsine and aluminium chloride gave precisely similar results.

(b) *Conversion into tetraphenylarsonium salts.* The tetraphenylarsonium iodide described by Chatt and Mann has an indefinite m. p. (decomp.), and the arsonium ion was therefore identified as the picrate and thiocyanate. When hot alcoholic solutions of the arsonium bromide or iodide and of picric acid were mixed and cooled, *tetraphenylarsonium picrate* separated as yellow crystals (alcohol), m. p. 201—202° (Found: C, 58·8; H, 3·8; N, 7·0. $C_{30}H_{22}O_7N_3As$ requires C, 58·9; H, 3·6; N, 6·9%). Addition of potassium thiocyanate to hot aqueous solutions of the bromide or iodide gave on cooling long colourless needles of the *thiocyanate*; these were redissolved in hot water, reprecipitated with potassium thiocyanate, and crystallised from water; m. p. 268—270° with preliminary softening (Found: C, 68·3; H, 4·9; N, 3·3. $C_{25}H_{20}NSAs$ requires C, 68·0; H, 4·6; N, 3·2%).

Reaction in Absence of Bromobenzene.—Many experiments were performed in which equimolecular mixtures of triphenylarsine and pure aluminium chloride were heated for various periods at various temperatures. Below *ca.* 250° no free arsenic and only traces of arsonium salt and of benzene were detected even after 2·5 hours' heating; the usual aqueous extraction of the almost colourless product furnished unchanged arsine and sometimes traces of arsine oxide formed by atmospheric oxidation. At temperatures above 280°, thermal decomposition became increasingly prominent; *e.g.*, a mixture of the arsine (10 g.) and aluminium chloride (4·5 g., 1 mol.) was slowly heated to 300°, no change being perceptible to *ca.* 280°; during 3 hours' heating at 300° effervescence and charring with deposition of arsenic proceeded, and the final product yielded benzene (2·3 g., identified by b. p. and as *m*-dinitrobenzene, m. p. 91°) and the arsonium iodide (0·5 g.).

When a similar mixture prepared, however, with impure aluminium chloride was heated, brisk evolution of benzene (identified as before) started at 120° and all reaction appeared complete after 0·5 hour's heating at 210—220°; the dark product now yielded the arsonium iodide (4·1 g.), identified as the picrate, m. p. 200—201°. In a repetition of the latter experiment, steam-distillation of the dark product did not produce any diphenyl.

Reaction in Presence of Bromobenzene.—(i) A mixture of the arsine (10 g.), pure aluminium chloride (4·5 g., 1 mol.), and bromobenzene (6·0 g., 1·2 mols.) was heated at 200° for 2 hours. No benzene was evolved and the product remained colourless. The usual extraction gave the arsonium iodide (12 g., 72% of theory on equation 1), which afforded the picrate, m. p. 201—202°. (ii) When the proportion of aluminium chloride was doubled, much decomposition occurred and the yield of iodide fell to 7·2 g. (43%). (iii) When the proportion of aluminium chloride was unchanged and that of bromobenzene increased to 10 mols., heating in a bath at 200° gave little decomposition and the yield of iodide was 9·2 g. (55%). (iv) When experiment (i) was repeated using impure aluminium chloride (10 g., to allow for hydrolysis), much decomposition and benzene evolution occurred, and the yield of iodide was 0·3 g. (v) Repetition of experiment (i) using, however, aluminium bromide instead of the chloride gave the same result as in (i).

All the above experiments involving mixtures of the arsine and pure aluminium chloride were repeated upon the pure addition product $[Ph_3As\rightarrow AlCl_3]$, and precisely similar results were obtained.

Mixed Arsonium Salts.—(i) After mixtures of triphenylarsine (2 g.), pure aluminium chloride (0·9 g., 1 mol.), and *p*-bromotoluene (2 g., 1·8 mol), or of diphenyl-*p*-tolylarsine (2 g.), the pure trichloride (0·83 g., 1 mol.), and bromobenzene (3·0 g., 3 mols.), had been heated at 180° for 1 hour, the usual extraction gave *triphenyl-p-tolylarsonium iodide* as a white crystalline stable *monohydrate*, m. p. 186—187°, which, however, on heating at 130°/15 mm. for 8 hours gave the anhydrous iodide (Found, for the hydrate: C, 55·3; H, 4·6; I, 23·6. $C_{25}H_{22}IAs,H_2O$ requires C, 55·3; H, 4·5; I, 23·4%. Found, for the anhydrous salt: C, 57·5; H, 4·6; I, 24·1. $C_{25}H_{22}IAs$ requires C, 57·3; H, 4·2; I, 24·2%). The iodide in turn gave a *thiocyanate* (water), long colourless needles of a polyhydrate which, in a vacuum over phosphoric anhydride, rapidly decrepitated to a stable *monohydrate* (m. p. 147—148°), which when kept at 130°/15 mm. for 10 hours gave the anhydrous thiocyanate (Found, for the monohydrate: C, 65·7; H, 5·1. $C_{26}H_{22}NSAs,H_2O$ requires C, 65·9; H, 5·1%. Found, for the anhydrous salt: C, 69·0; H, 4·8. $C_{26}H_{22}NSAs$ requires C, 68·6; H, 4·9%).

(ii) A mixture of diphenyl-*p*-tolylarsine (2 g.), pure trichloride (0·83 g.), and *p*-bromotoluene (2 g., 1·8 mol.), heated at 180° for 1 hour, similarly gave *diphenyldi-p-tolylarsonium iodide*, m. p. 194—195°, as a *hydrate* stable in a vacuum over phosphoric anhydride but giving the anhydrous salt at 130°/15 mm. (Found, for the hydrate: C, 55·0; H, 4·8; I, 22·2. $C_{26}H_{24}IAs,1{\cdot}5H_2O$ requires C, 55·2; H, 4·8; I, 22·5%. Found, for the anhydrous salt: I, 23·7. $C_{26}H_{24}IAs$ requires I, 23·6%).

(iii) A mixture tri-*p*-tolylarsine (2 g.), the pure trichloride (1 g., 1·3 mols.), and bromobenzene (15 g., 16·6 mols.), refluxed for 1 hour, gave *phenyltri-p-tolylarsonium iodide* (water), m. p. 205—206° after drying at 130°/15 mm. (Found: C, 58·5; H, 4·6; I, 22·8. $C_{27}H_{24}IAs$ requires C, 58·7; H, 4·7; I, 23·0%). This gave a hydrated thiocyanate (water), which after 8 hrs. at 80°/15 mm. gave the anhydrous *thiocyanate*, m. p. 143—144° (Found: C, 69·8; H, 5·6; N, 3·0. $C_{28}H_{24}NSAs$ requires C, 69·6; H, 5·4; N, 2·9%).

(B) *Trichlorodiphenylchloroarsinealuminium* $[Ph_2ClAs\rightarrow AlCl_3]$.—Pure powdered aluminium chloride (3 g., 1·2 mols.) was added to a solution of the chloroarsine (5·0 g., 1 mol.) in pure carbon disulphide (50 c.c.). On vigorous shaking, the aluminium chloride almost completely dissolved and a heavy pale brown oil separated. The supernatant disulphide was decanted, and the oil filtered rapidly under pressure, washed with carbon disulphide, and finally confined in a vacuum until free from the disulphide. The *addition product* formed a viscous syrup which was rapidly attacked by air, and hence the above operations were conducted as speedily as possible (Found: C, 34·6; H, 2·7; Cl, 35·8. $C_{12}H_{10}Cl_4AsAl$ requires C, 36·2; H, 2·5; Cl, 35·7%. Consistent carbon analyses could not be obtained).

(i) A mixture of diphenylchloroarsine (5 g.) and pure aluminium chloride (2·5 g., 1 mol.) was heated at 200° for 2 hours. No benzene was evolved but arsenic (0·6 g.) was deposited. Extraction gave a yellow sample of the arsonium iodide (3·7 g.), which after recrystallisation gave the pure arsonium picrate; the yields of arsenic and arsonium iodide were 84% and 77% of those required by equation (2). Steam-distillation of the reaction product gave no diphenyl. (ii) A repetition of (i) with heating at 150—160° for 2 hours gave a low yield of arsonium iodide (1·2 g., 25%) and much unchanged arsine. (iii) A repetition of (i) in which the temperature was increased slowly to 280° gave an evolution of benzene which was slight at 220° and copious at 280°; purification of the arsonium iodide required, however, many recrystallisations. (iv) Repetition of (i) with addition of bromobenzene (6 g., 2 mols.) to the mixture gave a product which furnished no arsonium salt and very little arsenic. (v) On repetition of (i) but with impure aluminium chloride which had been exposed for 10 mins., benzene (0·7 g.) was evolved as the temperature reached 100—120°; final heating at 200° for 2 hours gave arsenic (0·4 g., 57%) and the arsonium iodide (2·7 g., 56%). (vi) Another repetition using the trichloride which had been exposed for 0·5 hour gave benzene (1·8 g.), some arsenic trichloride, but no arsonium iodide.

When the addition product [$Ph_2ClAs \rightarrow AlCl_3$] replaced the monochloro-arsine and pure trichloride in experiments (i), (ii), and (iii), the same results were obtained.

(C) *Trichlorotris(phenyldichloroarsine)aluminium*, [$(PhCl_2As)_3AlCl_3$].—When pure powdered aluminium chloride (6·0 g., 1 mol.) was shaken with a solution of the dichloroarsine (10 g., 1 mol.) in carbon disulphide (50 c.c.), a dark brown oil separated but much aluminium chloride remained unchanged. The clear supernatant solvent was removed, and the oil filtered rapidly under suction to remove excess aluminium chloride, and confined in a vacuum until free from disulphide (Found: C, 26·1; H, 2·3; Cl, 39·9. $C_{18}H_{15}Cl_9As_3Al$ requires C, 26·9; H, 1·9; Cl, 39·8%). The oil undergoes rapid surface oxidation when exposed to air. The same product was obtained when the oil was thoroughly washed with carbon disulphide before vacuum treatment (Cl, 39·9%) and when an excess of aluminium chloride (3 mols.) was used in the above preparation (Cl, 40·0%). When, however, an excess of arsine was used, the addition product retained some free arsine in solution; *e.g.*, the use of 2 and 4 mols. of arsine gave products having Cl, 37·9 and 34·2%, respectively.

(i) A mixture of phenyldichloroarsine (5 g.) and pure aluminium trichloride (3 g., 1 mol.) was heated at 200° for 2 hours. At 160—180° arsenic chloride was evolved and arsenic liberated. The arsenic chloride was collected and redistilled; b. p. 129—130° (Found: Cl, 58·5. Calc. for $AsCl_3$: Cl, 58·7%). The main product, extracted as usual, gave a crude yellow arsonium iodide (2·5 g., 88% of that indicated by equation 3; picrate, m. p. 200°) and elementary arsenic (0·35 g., 21% of that present in the original arsine). No benzene could be detected. (ii) When the above mixture, after being heated as described, was heated at 280° for another hour, the products were the same but the iodide less pure. (iii) Repetition of (i) but with impure aluminium chloride gave vigorous evolution of benzene (1·1 g.) from 100° upwards. (iv) Repetition of (i) and (ii) upon the pure addition product gave identical results.

It is noteworthy that tetraphenylarsonium bromide, after being heated with aluminium chloride (4 mols., pure or impure) at 200° for 2 hours and then 280° for 1 hour, was recovered unchanged.

Triphenylarsine Oxide and Hydroxybromide.—When (i) a mixture of triphenylarsine oxide (2 g.) and aluminium chloride (2 g.) was heated at 250° for 3 hours, (ii) the same mixture was boiled with bromobenzene (15 g.) under reflux for 3 hours, (iii) the hydroxybromide (2 g.), aluminium chloride (2 g.), and bromobenzene (3 g. or 15 g.) were heated at *ca.* 200° for 3 hours, the product in each case, extracted as usual, gave the arsine hydroxy-iodide, which in turn gave the hydroxy-picrate, m. p. 168° (mixed and unmixed).

Tri-o-*tolylarsine.*—A mixture of the arsine (2 g.), aluminium chloride (2 g., 2·6 mols.), and *o*-bromotoluene was heated at 100° for 5 hours. Extraction with water, followed by sodium bromide treatment, gave the *hydroxy-oxybromide* (I) (water), m. p. 148—152° (preliminary softening) (Found: C, 62·0; H, 5·5; Br, 9·8. $C_{42}H_{43}O_3BrAs_3$ requires C, 62·3; H, 5·3; Br, 9·9%). Crystallisation of (I) from hot dilute hydrobromic acid gave the *oxydibromide* (II), colourless plates, m. p. 232° (preliminary softening) (Found: C, 57·7; H, 5·0; Br, 18·2. $C_{42}H_{42}OBr_2As_2$ requires C, 57·8; H, 4·9; Br, 18·3%). Treatment of (I) or (II) in hot alcoholic solution with picric acid gave the *oxydipicrate*, m. p. 169—171° (alcohol) (Found: N, 7·2. $C_{54}H_{46}O_{15}N_6As_2$ requires N, 7·2%). The above bromides were precipitated because the iodides separated as viscous solids which only slowly crystallised; the pure (I), treated in aqueous solution with potassium iodide, gave the *hydroxy-oxyiodide*, which was recrystallised from dilute potassium iodide solution containing sodium sulphite; colourless crystals, decomp. on heating (Found: I, 14·8. $C_{42}H_{43}O_3IAs_3$ requires I, 14·8%).

The experiment was repeated with variations of the aluminium chloride and *o*-bromotoluene proportions, the temperature, and the time of heating. Either the above oxidation or (particularly at higher temperatures) extensive decomposition occurred.

Tri-p-*tolylarsine.*—A mixture of the arsine (2 g.), pure aluminium chloride (0·8 g., 1 mol.), and *p*-bromotoluene (3·0 g., 3 mols.) was heated at 180—200° for 1 hour. The usual extraction followed by potassium iodide treatment gave *tetra*-p-*tolylarsonium iodide*, colourless needles (water), m. p. 253—255° (Found: C, 59·6; H, 5·0; I, 22·0. $C_{28}H_{28}IAs$ requires C, 59·4; H, 5·0; I, 22·4%). This compound, treated with excess potassium thiocyanate, gave the *thiocyanate* as a *monohydrate* (water), m. p. 207—209°, which lost water when heated at 130°/15 mm. for 10 hours (Found, for the hydrate: C, 67·2; H, 5·8; N, 2·8. $C_{29}H_{28}NSAs,H_2O$ requires C, 67·5; H, 5·8; N, 2·7%. Found, for the anhydrous salt: C, 69·8; H, 5·7. $C_{29}H_{28}NSAs$ requires C, 70·0; H, 5·6%).

Tri-m-*tolylarsine.*—Repetition of the previous experiment but with *m*-tolylarsine and heating for 2·5 hours gave *tetra*-m-*tolylarsonium iodide* (water), m. p. 155—156° (Found: C, 59·4; H, 5·2; I, 22·7%). Heating the mixture at 120° for 4 hours and subsequent treatment with sodium bromide gave only tri-*m*-tolylarsine hydroxybromide (crystallised from dilute hydrobromic acid), m. p. 188° (Found: Br, 18·6. Calc. for $C_{21}H_{22}OBrAs$: Br, 18·0%).

Tri-o-*tolylphosphine.*—Mixtures of this phosphine with aluminium chloride and *o*-bromotoluene in various proportions, heated under widely different conditions, appeared to undergo almost complete decomposition, neither the phosphine hydroxy-halide nor the phosphonium salt being isolated.

Tri-p-*tolylphosphine.*—A mixture of the phosphine (3 g.), pure aluminium chloride (3 g., 2·3 mols.), and excess *p*-bromotoluene (15 g., 9 mols.), boiled under reflux for 1 hour, gave ultimately *tetra*-p-*tolylphosphonium iodide*, colourless needles (water), m. p. 260—264° (Found: C, 64·4; H, 5·7; I, 24·2. $C_{28}H_{28}IP$ requires C, 64·3; H, 5·4; I, 24·3%).

Tri-m-*tolylphosphine.*—A mixture of the phosphine (3 g.), pure aluminium chloride (1·3 g., 1 mol.), and *m*-bromotoluene (4 g., 2·4 mols.), heated at 190—200° for 2 hours, gave the *phosphonium iodide*, colourless crystals (water), m. p. 175—176° (Found: C, 64·5; H, 5·2; I, 24·5%). The m. p.'s of both these iodides must be determined by rapid heating: slow heating causes darkening, which will occur even on exposure to the light at room temperature. The phosphonium iodides are all markedly less stable than their arsonium analogues in this respect.

Tetraphenylphosphonium thiocyanate (water), colourless needles, unaffected by heating to 270°, was prepared from the iodide (Found: C, 75·3; H, 5·0; N, 3·5. $C_{25}H_{20}NSP$ requires C, 75·5; H, 5·1; N, 3·5%).

Toxic Properties.—Dr. Busvine reports: "The samples, which were white crystalline powders, were not readily soluble in mineral oil which would be the most satisfactory vehicle. Volatile solvents would leave them deposited as solids, so they were tested rather crudely in this form. Tapes thoroughly dusted with the crushed crystals were put

into tins with lice. Some samples killed a high proportion of lice but all were slow in comparison to ordinary naphthalene. A proportion of eggs laid on the tapes hatched in all cases.

Results.—

Compound.	Day: Deaths of 6 adult lice. 1.	2.	3.	Eggs. No. laid.	% hatched.
Tetraphenylphosphonium thiocyanate	0	1	0	10	80
Tetraphenylphosphonium iodide	0	5	1	31	52
Tetraphenylarsonium thiocyanate	2	3	0	19	58
Tetraphenylarsonium iodide	1	4	0	5	40
Tetraphenylstibonium iodide	0	3	3	16	75
Naphthalene	6	—	—	0	—

Although the tests were rather crude, they show that the compounds are not good insecticides for lice."

We are indebted to Trinity College for a Dunning Scholarship (D. R. L.).

THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 6th*, 1942.]

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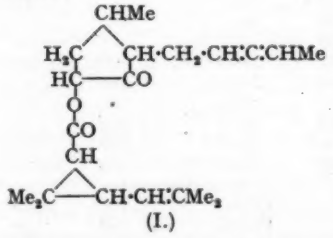
139. *Absorption Spectra and the Structures of Pyrethrins I and II.*

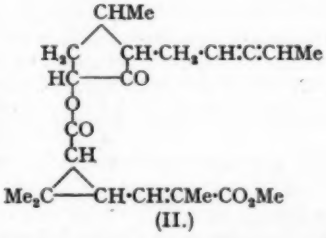
By A. E. GILLAM and T. F. WEST.

Absorption-spectra data on pyrethrins I and II and related compounds are recorded and discussed in relation to the molecular structures of the compounds. Utilising stepwise hydrogenation with absorption-spectra control, we have obtained results which lead to the following conclusions: (*a*) In the pyrethrolone fragment of the pyrethrin molecules two *separate* chromophoric systems are present each containing more than one double linkage; it follows, therefore, that the trienone chromophoric system which has been postulated (V) cannot be present. (*b*) An $\alpha\beta$-unsaturated ketone grouping is present in a five-atom ring. (*c*) The unsaturation in the side chain is present as a conjugated diene, the presence of a cumulated diene system being precluded by the absorption-spectra evidence.

These conclusions necessitate reconsideration of the structure of the pyrethrolone fragment and either a change in the location of the unsaturation in the side chain or a revision of the position of the unsaturated ketone chromophore in the five-atom ring. The effects of these conclusions on the structures of these compounds have been tentatively discussed.

THE structural formulæ (I) and (II) assigned to pyrethrin I and pyrethrin II by Staudinger and Ruzicka (*Helv. Chim. Acta*, **1924**, **7**, 177) involved for pyrethrolone a *cyclo*pentanolone structure (III) having as one substituent the allene group $\cdot CH_2 \cdot CH{:}C{:}CHMe$ not previously suspected in naturally occurring compounds. The chemical evidence advanced for the allene side chain depended mainly on the production of acetaldehyde on ozonolysis, formaldehyde being produced only in negligible quantity, whereas oxidation of the ozonolysis products with hydrogen peroxide gave malonic acid among other products. With potassium permanganate, acetic acid was produced.


(I.)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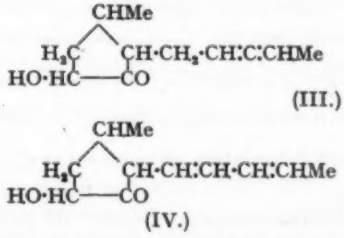
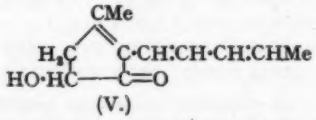
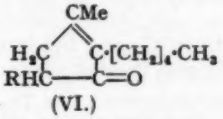

(III.)

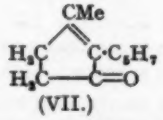
(IV.)

Subsequently, Ruzicka and Pfeiffer (*ibid.*, **1933**, **16**, 1208) reconsidered the data and proposed the more frequently encountered conjugated system for the side chain (IV), with the observation " dass über der Lage der Doppelbindungen beim Pyrethrolone noch eine gewisse Unklarheit herrscht."

On the basis of analyses of pyrethrolone, tetrahydropyrethrolone, and their derivatives, LaForge and Haller (*J. Amer. Chem. Soc.*, **1936**, **58**, 1061, 1777) replaced the *cyclo*pentanolone by a *cyclo*pentenolone nucleus so that, Ruzicka and Pfeiffer's conjugated side chain being adopted, a trienone system was involved for pyrethrolone (V) and tetrahydropyrethrolone was formulated as (VI, R = OH).


(V.)


(VI.)


(VII.)

Proof of the formula of the latter was confirmed by its conversion into tetrahydropyrethrone (LaForge and Haller, *J. Amer. Chem. Soc.*, **1936**, **58**, 1777), which was shown to be identical with dihydrojasmone (VI, R = H) of established constitution (Ruzicka and Pfeiffer, *loc. cit.*; Treff and Werner, *Ber.*, **1933**, **66**, 1521). It was pointed out by LaForge and Haller (*loc. cit.*) that the formation of malonic acid as a degradation pro-

duct of the side chain, which was considered to prove the presence of the grouping $-CH{\cdot}CH_2{\cdot}CH-$ in the pyrethrolone side chain (III), may possibly have arisen through oxidation of the nucleus (V).

In further work, however, LaForge and Haller (*J. Org. Chem.*, 1938, **2**, 546) were unable to obtain proof of the presence of either the cumulated or the conjugated system, but regarded the only uncertainty in the formula of pyrethrone to be in the position of one of the two ethylene linkages—since the formation of acetaldehyde on ozonolysis appeared to fix one linkage. In fact, therefore, LaForge and Haller considered that the only difficulty involved was the decision between position 2, 3 (III) or 1, 2 (IV) for the second double bond, with the reservation, however, that " The possibility of the presence of a second ring system that is easily cleaved by hydrogenation, with the formation of a saturated five-membered straight chain, cannot be excluded from consideration."

Subsequent work by Acree and LaForge (*J. Org. Chem.*, 1939, **4**, 569; 1940, **5**, 48, 430), involving the synthesis of allenes for a study of their behaviour towards certain reagents in comparison with that displayed by pyrethrolone and its deoxy-derivative, pyrethrone (VII), provided some indirect evidence for the presence of the cumulated double bonds in the side chain but the issue remained in doubt.

Applying the principles of LaForge and Haller (*J. Amer. Chem. Soc.*, 1935, **57**, 1893), we have readily prepared concentrates containing 80% of pyrethrin II similar to those obtained by those authors, but by introducing suitable modifications we prepared concentrates of pyrethrin I containing 70% of the active principle whereas they reported their concentrates to contain not more than 55% of this compound (*J. Org. Chem.*, 1937, **2**, 49).

It was found that, whereas pyrethrin II can be regenerated from its semicarbazone to provide the pure ester, yet some decomposition occurred during regeneration from pyrethrin I semicarbazone although the absorption data for the original pyrethrin I and II concentrates before conversion into the semicarbazones and after regeneration indicated that the chromophoric system was unaltered.

TABLE I.

Absorption Spectra of Pyrethrins I and II and related compounds.

(*Alcoholic solutions.*)

	Purified samples.		Preliminary samples.		
	$\lambda_{max.}$	ε.	$\lambda_{max.}$	ε.	M.W. used.
Pyrethrin I	2270	29,000	2280	24,000	328
Pyrethrin II	2310	35,400	2310	33,000	372
Tetrahydropyrethrin II	2365	24,600	—	—	376
Pyrethrolone (from pyrethrin I)	2280 3085	27,000 96	— —	— —	178 —
Pyrethrolone (from pyrethrin II)	2280	25,800 *	2280	23,700 *	178
Pyrethrolone (from mixed pyrethrins)	2270 (3080) †	26,700 96	2285 (3000)	19,500 178	178 —
Tetrahydropyrethrolone (from pyrethrin I)	2320 3120	11,600 64	— —	— —	182 —
Tetrahydropyrethrolone (from pyrethrin II)	2320	12,800 *	—	—	182
Dihydrojasmone	2370 3040	12,200 55	— —	— —	— —
Pyrethrin I semicarbazone	2290 2670	21,400 21,100	2300 2665	20,000 20,500	385 —
Pyrethrin II semicarbazone	2360 (2660)	31,200 24,000	2355 2640	33,400 26,200	397 —
Pyrethrolone semicarbazone (from pyrethrin I)	2320 2655	20,100 19,500	2290 2655	21,760 19,800	235 —
			Purified samples.		
Pyrethrolone semicarbazone (from pyrethrin II)	—	—	2310 2650	22,300 20,200	235 —
Tetrahydropyrethrolone semicarbazone (from pyrethrin I)	—	—	2650	22,500	239
Tetrahydropyrethrolone semicarbazone (from pyrethrin II)	—	—	2650	21,770	239
Dihydrojasmone semicarbazone	—	—	2665	20,400	—
Tetrahydropyrethrin II semicarbazone	—	—	2620 (2385)	26,200 20,600	401 —

* Ketone band not examined.

† Inflexions on the absorption curves are indicated by parentheses round the values of $\lambda_{max.}$

The main object of the present paper is to record absorption-spectra data on pyrethrins I and II and their derivatives * and to consider their bearing upon the molecular structures of these compounds.† The numerical data are collected in Table I, a few items only being presented as absorption curves (Figs. 1 and 2).

It is notable that pyrethrin I, pyrethrin II, and the pyrethrolone obtained from either have very similar absorption spectra. Hence, it can be inferred that all three compounds contain similar chromophoric systems,

* After nearly completing this work we discovered that Dr. LaForge and his collaborators at the United States Bureau of Insecticides contemplated using absorption-spectra methods in work on the pyrethrins. We communicated with Dr. LaForge and offered to withhold our results for the present, but he informed us that he was not extending the absorption-spectra side of his work and very kindly invited us to publish our results when ready.

† The highly intense absorption bands of the pyrethrins and the five-atom-ring ketone, pyrethrolone, should offer the basis of a useful additional method of determination and control for biological purposes, and this aspect of the work will be dealt with elsewhere.

and that, in transforming the pyrethrins into pyrethrolone, no major change of structure involving the chromophoric groups can have occurred.

The Swiss and the American workers having approximately determined the structures of these compounds by chemical work, we now attempt to draw inferences from absorption-spectra data as to the distribution of the unsaturated linkages in the several molecules, since the exact location of some of these linkages remains in doubt.

Let us consider the postulated structures from the point of view of the presence of light-absorbing groups. The first of the chromophores is attached to the three-atom ring in each of the pyrethrins. In pyrethrin I it is a single ethylene linkage (I), which should give rise to an absorption band situated below 2000 A. and can therefore be neglected in work with a quartz spectrograph which is limited to the range *ca.* 2150—7700 A. The corresponding chromophore in pyrethrin II [·CH:CMe·CO_2Me; cf. (II)], although a conjugated one, would be expected to give rise to a band situated on the extreme edge of the quartz ultra-violet region by analogy with crotonic acid which, with a similar chromophoric group, exhibits $\lambda_{max.}$ at 2080 A. ($\varepsilon = 12{,}200$). This grouping also can therefore be ignored in the present work.

This leaves us with three main possibilities for the other chromophoric groups: (*a*) a cumulated system of two ethylene linkages, ·CH:C:CHMe, with an isolated C:C·C:O chromophore in addition; (*b*) a C:C·C:C system in crossed conjugation with a C:C·C:O group; and (*c*) a C:C·C:C system unconjugated with a ·C:C·C:O group (this suggestion has not been advanced previously but must be considered).

In considering the absorption spectra of a compound containing several chromophoric groups it is helpful if the chromophores can be eliminated one by one, and the absorption spectra of the simpler absorbing entities examined separately. With the pyrethrins, the first stage in this process is to convert them into pyrethrolone, thus eliminating the chain containing the C:C link (pyrethrin I) or the C:C·CO_2Me group (pyrethrin II). The fact that the absorption spectra of the two pyrethrins are closely similar to that of the pyrethrolone derived from them (Table I) further justifies the above assumption that the two chromophoric groups just mentioned can be ignored.

The next stage in the process is to remove some of the unsaturation and examine the absorption spectra due to the thus simplified chromophoric groups. It happens that when pyrethrolone is hydrogenated with a platinum catalyst a good yield of the tetrahydro-derivative is obtained, two ethylene linkages being saturated. The absorption spectrum of the product (cf. Table I and Fig. 1, where only the *K*-band is shown) is typical of that of an αβ-unsaturated ketone and consistent with formula (VI, R = OH). The intense band is situated at shorter wave-lengths than is to be expected for a trisubstituted αβ-unsaturated ketone (Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123) but it has been shown (Gillam and West, this vol., p. 487) that the five-atom ring environment displaces the maximum of the *K*-band to shorter wave-lengths and to approximately the same extent in other five-atom ring compounds (dihydrojasmone and *iso*thujone).

We now have the observed facts that when two ethylene linkages in pyrethrolone are removed by hydrogenation the resulting tetrahydro-compound exhibits an absorption spectrum typical of that of an αβ-unsaturated ketone in a five-atom ring environment, and further, that the absorption maximum of the tetrahydro-compound is located at a wave-length not far removed from that of the original pyrethrolone. Although we have not yet found a model substance having the crossed conjugated system as postulated in (V), its absorption spectrum might be expected to be closer to that of a conjugated triene than a conjugated diene, in which case it should absorb at distinctly longer wave-lengths than the observed 2300 A. (seven trienes which have been examined, including hexatriene, calciferol, and tachysterol, absorb maximally between 2550 and 2800 A.; cf. Koch, *Chem. and Ind.*, 1942, **61**, 273).

It can thus be inferred that the chromophoric group containing the two ethylene linkages in the side chain of pyrethrolone is not conjugated with the C:C·C:O group, and that the absorption spectrum of pyrethrolone is in fact a summation of the absorption due to C:C·C:O and that due to the two ethylene linkages (whether cumulated or conjugated). This inference is strongly supported by the observation that in the semicarbazone of pyrethrolone part of the absorption is displaced to 2650 A., which is usual with the semicarbazones of C:C·C:O compounds in general. In pyrethrins I and II also there is residual absorption near 2300 A. which is not affected by semicarbazone formation, and this should therefore be due to the isolated non-ketonic chromophore (cf. Fig. 2).

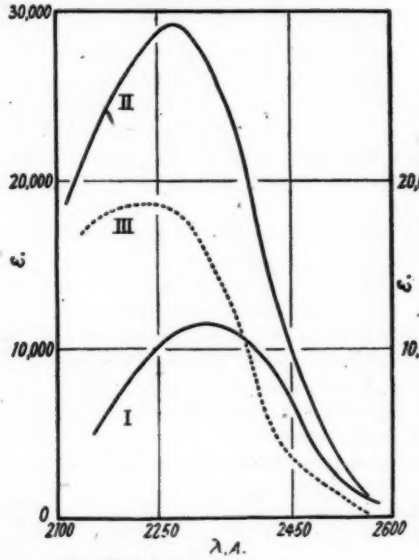
Having thus isolated the C:C·C:O chromophore by hydrogenation of pyrethrolone, we now have to isolate and examine the absorption due to the two ethylene linkages in the side chain, and we do this indirectly as follows. Accepting as proven that the two chromophores are in fact isolated and that their absorption will therefore be a summation, we have a record of the absorption due to the two chromophores together and to the C:C·C:O separately. Then the absorption due to the two ethylene linkages should be given by the arithmetical difference between these two curves, since unconjugated chromophores produce additive effects only. The observed curves and the subtraction curve for the pair of compounds pyrethrolone and tetrahydro-pyrethrolone are shown in Fig. 1.

The point now at issue is whether these double bonds are cumulated or conjugated. Now we know that acyclic dienes, either open-chain or with one cyclic substituent, absorb between 2170 and 2365 A. (Booker, Evans, and Gillam, J., 1940, 1453) with ε ranging from 5,000 to 25,000. The subtraction curve shows $\lambda_{max.}$ near 2275 A., with $\varepsilon = 18{,}600$, data which are thus absolutely typical of a conjugated diene. On the other hand, cumulated dienes are only weakly absorbing substances; *e.g.*, ethylallene exhibits an inflection only

near 2270 A., with ε = only 900 approx. (Carr and Stücklen, quoted by Burr and Miller, *Chem. Rev.*, 1941, **29**, 419), whilst keten and diethylketen containing the analogous cumulated C:C:O system have values of ε at 2270 A. of order only 28 and 280 respectively (I.C.T., Vol. V).

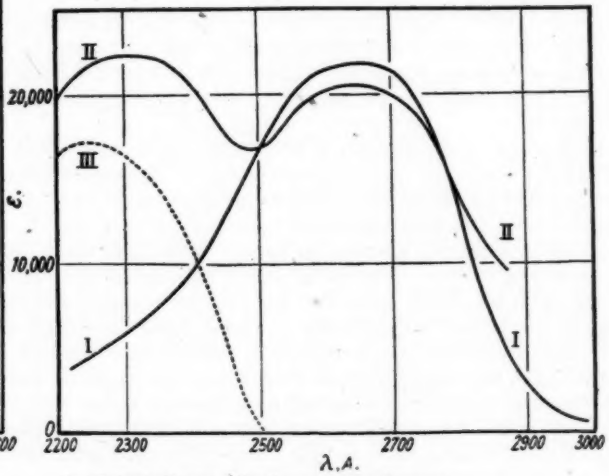
The absorption due to the diene can be obtained independently from other data presented here by a subtraction method using the observed absorption of the semicarbazones of pyrethrolone and tetrahydropyrethrolone. This is shown in Fig. 2. The subtraction curve of the ketones gives $\lambda_{max.}$ 2275 A. (ε = 18,600) for the absorption of the diene component, whilst the corresponding value from the semicarbazones is $\lambda_{max.}$ 2245 A. (ε = 17,200). The two independent results are in good agreement with each other, and after comparison of the light-absorption of *cumulated* dienes with that of *conjugated* dienes there can be no doubt that the two ethylene linkages in the C_5 side chain of pyrethrolone and its semicarbazone are conjugated and not cumulated. This is also consistent with experience that cumulated systems of ethylene linkings have not so far been observed in natural products. The possible criticism that there may have been a change from a cumulated to a conjugated system in passing from pyrethrin to pyrethrolone is not valid, since (as already pointed out) the absorptions of both the pyrethrins and pyrethrolone are so alike as to preclude changes of structure involving the chromophoric groups.

FIG. 1.



I. *Tetrahydropyrethrolone.*
II. *Pyrethrolone.*
III. *Subtraction curve* (II—I) *equals the absorption of the diene component in pyrethrolone.*

FIG. 2.



I. *Tetrahydropyrethrolone semicarbazone.*
II. *Pyrethrolone semicarbazone.*
III. *Subtraction curve* (II—I) *equals absorption of diene component in pyrethrolone.*

Absorption spectra in alcohol.

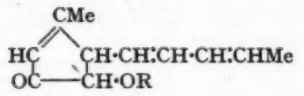
Since the absorption data so clearly indicate the presence of two separate conjugates in pyrethrolone, the possibility of a second ring cleaved by hydrogenation as postulated by LaForge (*loc. cit.*) appears to be ruled out of consideration.

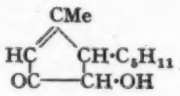
We have just seen that two independent but indirect determinations of the light absorption due to the diene chromophore in pyrethrolone give values of $\lambda_{max.}$ of 2245 and 2275 A. respectively. This gives an average value of 2260 $\pm$ 15 A. (average ε = 17,900). If we apply Woodward's empirical method of predicting the absorption spectrum of a conjugated diene (*loc. cit.*), we can calculate that for an unsymmetrical disubstituted diene of the type CHR:CH·CH:CHMe the absorption band should lie at 2270 A., which compares well with the 2260 $\pm$ 15A. observed. It should be noted, however, that the estimated value for $CH_2R{\cdot}CH{:}CH{\cdot}CH{:}CH_2$ comes to 2220 A., which is not very significantly different.

The general conclusions reached above are supported by an examination of the Ponndorf–Meerwein *reduction product* of pyrethrolone methyl ether, which shows maximum absorption situated at nearly the same wavelength as that of the methyl ether itself but at a reduced intensity. This observation precludes the presence of a conjugated triene system in the reduced product, and therefore presumably in the original pyrethrolone.

If the jasmone ring structure is accepted, then the only possible formulæ for the pyrethrins must contain the $\cdot CH_2{\cdot}CH{:}CH{\cdot}CH{:}CH_2$ side chain; but this involves the assumption that during ozonolysis the terminal double linkage migrates, leaving the grouping :CHMe which is necessary to explain the production of acetaldehyde. On the other hand, if the terminal group :CHMe be accepted, revision of the *cyclo*pentenolone ring becomes necessary, and this in turn involves the assumption that during the production of dihydrojasmone (VI, R = H) by hydrogenation an isomerisation occurs. This is only possible if a tentative structure (VIII),

which is in accordance with the absorption data, be assigned to the pyrethrolone fragment of the pyrethrin molecules.

(VIII.) 

 (IX.)

A similar change must then be assumed to take place during the preparation of dihydrojasmone from tetrahydropyrethrolone *via* the chloro-compound which LaForge and Haller (*J. Amer. Chem. Soc.*, 1936, **58**, 1777) formulated as (VI; R = Cl). In this connection it may be significant that tetrahydropyrethrolone shows maximum absorption at 2320 A., whereas dihydrojasmone and *iso*thujone absorb at 2370 A. and 2375 A. respectively. Hence, tetrahydropyrethrolone would be more suitably formulated as the disubstituted αβ-unsaturated ketone (IX), which should absorb at a shorter wave-length than the corresponding trisubstituted systems of dihydrojasmone and *iso*thujone (cf. Woodward, *loc. cit.*; Gillam and West, this vol., p. 487). Although no chemical evidence appears to exist in support of this change, the fact that both pyrethrolone and tetrahydropyrethrolone are readily obtained in enolic forms (cf. Haller and LaForge, *J. Org. Chem.*, 1938, **3**, 543) clearly indicates the labile nature of the ring system. Furthermore, we have definite absorption-spectra evidence that tetrahydro*iso*pyrethrolone enol is tautomeric, since at a concentration (alcohol) of 0·0055% the absorption maximum is situated at 2540 A., whereas in 0·025% solution the maximum is displaced to 2460 A. We hope to investigate the absorption spectra of these enolic compounds more fully later.

Experimental.

Carbon and hydrogen determinations are by Drs. Weiler and Strauss, Oxford. Absorption data are only given here if they do not appear in the main table.

Purification of Pyrethrum Extract.—An extract (1360 g.) (containing pyrethrin I, 14·6%; pyrethrin II, 18·4% by the Wilcoxon–Holaday method), obtained by extracting Kenya pyrethrum flowers with light petroleum, was dissolved in acetone (cf. B.P. 493,074), the insoluble portion rejected, and the extract then purified according to LaForge and Haller (*J. Amer. Chem. Soc.*, 1935, **57**, 1893). In this manner two concentrates were obtained containing (*a*) pyrethrin II 79·6, pyrethrin I 17·1%, and (*b*) pyrethrin I 57·7, pyrethrin II 5·0%. The latter (120 g.) was dissolved in methyl alcohol (1275 ml.), and water (225 ml.) added in small quantities with efficient shaking. After standing overnight at 0°, the insoluble material was filtered off, the methyl alcohol removed from the filtrate by distillation under reduced pressure, and the oil which separated extracted with light petroleum; this solution was dried over sodium sulphate, and the solvent removed to give a product (65 g.) containing pyrethrin I 69·4, pyrethrin II 8·1% (Wilcoxon–Holaday). Further details of the method of purification and separation will be recorded elsewhere with notes on the Wilcoxon–Holaday and Seil methods of analysis as compared with the biological activity of various extracts.

Pyrethrin I and Derivatives.—The pyrethrin I concentrate (60 g.), dissolved in alcohol (220 ml.) and pyridine (135 ml.), and a solution of semicarbazide hydrochloride (36 g.) in hot water (45 ml.) were mixed and treated as described by Haller and LaForge (*J. Org. Chem.*, 1936, **1**, 47). The first crop of crystals, after being washed successively with 60% aqueous alcohol, dilute acid, water, and 85% alcohol and dried in a vacuum desiccator over calcium chloride, had m. p. 109° (sinter 96°) (54 g.). A second crop (7 g.), m. p. 107° (sinter 91°), was obtained by adding to the filtrate the alcoholic washings from the first crop and water (75 ml.). The first crop was recrystallised twice from alcohol, and crystals (31 g.) having m. p. 113° (sinter 104°), and a portion of this was used for the preparation of pyrethrolone. This product (7 g.) was again recrystallised twice from alcohol, and the pyrethrin I semicarbazone (3·9 g.) had m. p. 113° (sinter 108°) (Found: C, 67·5; H, 8·2. Calc. for $C_{22}H_{31}O_3N_3$: C, 68·6; H, 8·05%).

The semicarbazone (3 g.) was heated with oxalic acid (6 g.) in water (40 ml.) on the water-bath for 5 hours, agitation being achieved by a stream of carbon dioxide. The regenerated pyrethrin I (1·26 g.) obtained by extraction with light petroleum (Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 177; Haller and LaForge, *J. Org. Chem.*, 1936, **1**, 48) had $n_D^{18°}$ 1·5192, $[\alpha]_D$ − 32·3° (*c*, 5·66 in ether) (Found: C, 76·4; H, 8·9. Calc. for $C_{21}H_{28}O_3$: C, 76·8; H, 8·5%). It contained some pyrethrin II, and some decomposition appeared to have occurred during regeneration because it had a pyrethrin I content of only 65·4% and contained 6·3% of pyrethrin II (Wilcoxon–Holaday; the corresponding Seil figures were 70·5 and 8·0%).

The above semicarbazone, m. p. 113° (sinter 104°) (24 g.), was treated with 600 ml. of methyl alcohol and 45 ml. of 0·5N-sodium methoxide (Haller and LaForge, *J. Org. Chem.*, 1936, **1**, 50). After standing at room temperature for eight days and at 0° for 1 day crystals (8·2 g.) separated, and by concentration under reduced pressure and addition of water a second crop (4·1 g.) was obtained. The two crops were bulked, and recrystallised twice from methyl alcohol, 1 g. of insoluble material being rejected. The pyrethrolone semicarbazone (8 g.) had m. p. 210—211° (decomp.) (rapid heating) (Found: C, 61·0; H, 6·9. Calc. for $C_{13}H_{17}O_2N_3$: C, 61·3; H, 7·2%).

The pyrethrolone (1·05 g.) regenerated from this semicarbazone (3 g.) in the presence of cold potassium hydrogen sulphate solution and ether in an atmosphere of carbon dioxide (Haller and LaForge, *J. Amer. Chem. Soc.*, 1937, **59**, 1678) had b. p. 144°/1 mm., $n_D^{18°}$ 1·5390, $d_{19°}^{19°}$ 1·05, $[\alpha]_D$ + 14·1° (*c*, 6·23 in ether) (Found: C, 73·7; H, 8·3. Calc. for $C_{11}H_{14}O_2$: C, 74·15; H, 7·9%).

Pyrethrin II and Derivatives.—The pyrethrin II concentrate (35 g.) was dissolved in alcohol (117 ml.) and pyridine (51 ml.) and treated with a solution of semicarbazide hydrochloride (14·5 g.) in water (17·5 ml.); on standing at room temperature for 2 days the solution deposited a considerable bulk of crystals. Water (10 ml.) was now added with stirring, and the solution cooled to 0° for 36 hours. The crystals were washed successively with 60% alcohol, dilute acid, water, and 85% alcohol before being dried in a vacuum desiccator; the product (27·8 g.) had m. p. 162—163°. By adding the aqueous-alcoholic washings and water (47 ml.) to the filtrate and cooling to 0° overnight, a second crop (4·4 g.) was obtained, m. p. 150° (sinter 125°). The first crop was recrystallised twice from ether as described by Haller and LaForge (*J. Org. Chem.*, 1936, **1**, 44) and had m. p. 165° (Found: C, 64·6; H, 7·2. Calc. for $C_{22}H_{31}O_5N_3$: C, 64·3; H, 7·2%).

The pyrethrin II was regenerated by heating the semicarbazone (3 g.) with a solution of oxalic acid (6·2 g.) in water (42 ml.) at 100° for 5½ hours, agitation being ensured by a stream of carbon dioxide. The oil (1·15 g.) recovered by extraction with light petroleum had $n_D^{21·5°}$ 1·5290 (Found: C, 71·2; H, 7·55; OMe, 8·4. Calc. for $C_{22}H_{32}O_5$: C, 71·0; H, 7·5; OMe, 8·3%). This showed a pyrethrin II content of 99·0% by the Wilcoxon–Holaday, and 100·4% by the Seil method.

Pyrethrin II semicarbazone (15 g.), dissolved in methyl alcohol (60 ml.), was mixed with 0·5N-sodium methoxide (72 ml.) and water (3·6 ml.) (Haller and LaForge, *J. Org. Chem.*, 1936, **1**, 48). After standing at 0° for 6 days, a crop of crystals (6·9 g.) was obtained, and by treating the filtrate as described by Haller and LaForge, a further 1·15 g. The first crop was recrystallised twice from methyl alcohol (0·85 g. of insoluble material rejected), and the product (4·4 g.) had m. p. 212—213° (decomp.) (rapid heating) (Found: C, 61·5; H, 7·0%).

The pyrethrolone (0·8 g.) regenerated from this semicarbazone (3 g.) in the presence of a cold potassium hydrogen sulphate solution and ether had b. p. 156—158°/2 mm., $n_D^{19\cdot5°}$ 1·5422, $d_{16°}^{16°}$ 1·06, $[\alpha]_D$ + 14·2° (*c*, 3·87 in ether) (Found: C, 73·0; H, 8·15%).

Before purifying the larger quantity of extract referred to above, preliminary experiments were carried out with 450 g. of a similar pyrethrum extract (containing pyrethrin I, 14·4; pyrethrin II, 13·2%) and the derivatives and relevant details of preparation are recorded below, absorption data being in the foregoing table.

Preliminary Preparation of Pyrethrins and Derivatives.—A purified pyrethrin concentrate (pyrethrin I, 33·8; pyrethrin II, 47·2%) (50 g.) was dissolved in alcohol (200 ml.) and treated with a solution of semicarbazide hydrochloride (23 g.) and crystalline sodium acetate (37 g.) in water (36 ml.) (see Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 177). After standing for 2 days, the first crop (13·8 g.) when washed with 80% alcohol had m. p. 110° (sinter 96°). After recrystallising once from acetone and three times from alcohol the product had m. p. 116—118° (Found: N, 10·35. Calc. for $C_{22}H_{31}O_3N_3$: N, 10·9%). The pyrethrin I regenerated in the presence of oxalic acid solution had $n_D^{19\cdot5°}$ 1·5232 and contained pyrethrin I, 57·5; pyrethrin II, 15·8% (Wilcoxon–Holaday method). The second crop (5 g.), which separated on standing, had m. p. 104° (sinter 92°). This was converted into pyrethrolone semicarbazone by treatment with methyl alcohol (20 ml.), 0·5N-sodium methoxide (24 ml.), and water (1·2 ml.). The recrystallised pyrethrolone semicarbazone (1·5 g.) obtained had m. p. 208° (Found: N, 17·6. Calc. for $C_{13}H_{17}O_2N_3$: N, 17·9%). The regenerated pyrethrolone had $n_D^{20°}$ 1·5350. After removal of the second crop, the solution was concentrated under reduced pressure and extracted with ether to give a syrupy liquid (40 g.). This semicarbazone mixture was converted into pyrethrolone semicarbazone as described by Staudinger and Ruzicka (*loc. cit.*), and this after recrystallisation from acetone had m. p. 208° (decomp.). The constants and absorption of the regenerated ketone indicated that it was the purest sample obtained in our experiments [the difficulty of obtaining satisfactory analytical data for pyrethrolone and its tetrahydro-derivative has been stressed by LaForge and Haller (*J. Amer. Chem. Soc.*, 1936, **58**, 1777)]. It had b. p. 150°/1·5 mm., $n_D^{21°}$ 1·5410, $d_{20°}^{20°}$ 1·042, $[\alpha]_D$ + 19·9° (*c*, 3·912 in ether) (Found: C, 74·2; H, 8·0%).

A pyrethrin II concentrate (pyrethrin II, 81·6%; pyrethrin I, 5·9%) (2·7 g.) was converted as described by LaForge and Haller (*J. Org. Chem.*, 1936, **1**, 44) into pyrethrin II semicarbazone, m. p. 164—165° (Found: N, 9·7. Calc. for $C_{23}H_{31}O_3N_3$: N, 9·8%). The regenerated pyrethrin II showed $\lambda_{max.}$ 2310 A. (ε = 33,000).

Tetrahydropyrethrin II.—Pyrethrin II semicarbazone, m. p. 164—165° (4·93 g.), was hydrogenated in ethyl acetate with platinum oxide as catalyst (Haller and LaForge, *J. Org. Chem.*, 1936, **1**, 46). The solvent was removed by distillation, the residue dissolved in ether, and the ethereal solution washed successively with potassium carbonate solution (1%) and water and dried over sodium sulphate. After removal of ether, the oily residue (4·46 g.) quickly set to a solid, m. p. 130° (sinter 125°), and was recrystallised readily from *cyclo*hexane, but in order to remove the solvent from the crystals it was necessary to reflux them with light petroleum. The product thus obtained (3·3 g.) had m. p. 134° (sinter 124°) raised by recrystallisation from alcohol to 139—141° (Found: C, 63·3; H, 7·7. Calc. for $C_{23}H_{35}O_3N_3$: C, 63·7; H, 8·1%).

This semicarbazone (1·5 g.) was heated for 5 hours at 100° with oxalic acid (3 g.) in water (20 ml.), and the oil extracted with light petroleum. This solution was washed until neutral, dried, and kept at 0° for some hours to remove a small amount of unchanged semicarbazone. The oil obtained (375 mg.) by removing the solvent had $n_D^{23\cdot5°}$ 1·5115 (Found: C, 71·0; H, 8·7. Calc. for $C_{23}H_{33}O_3$: C, 70·2; H, 8·5%).

Reduction of Pyrethrolone Methyl Ether.—This ether (Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 212) had b. p. 110—113°/2 mm., $n_D^{21°}$ 1·5142, $\lambda_{max.}$ 2260 A. (ε = 28,800) (Found: C, 75·6; H, 8·9. Calc. for $C_{12}H_{16}O_2$: C, 75·0; H, 8·3%). A sample (5·2 g.) was reduced with aluminium *iso*propoxide (1·95 g.) in dry *iso*propyl alcohol (17 ml.), the constant-volume distillation being continued until the distillate no longer gave a test for acetone with 2 : 4-dinitrophenylhydrazine (6½ hours). The solution was subjected to steam distillation and a light petroleum extract of the distillate, washed and dried, yielded on distillation three fractions which appeared to be mixtures of the reduced product and unchanged pyrethrolone methyl ether:

Fraction.	B. p./1 mm.	Wt., g.	$n_D^{22°}$.	$\lambda_{max.}$.	$\varepsilon_{max.}$.	C, %.	H, %.
1	96—98°	0·78	1·5051	2260	17,500	73·6	8·9
2	100—103	1·12	1·5081	2270	20,000	73·3	9·0
3	103—108	1·67	1·5118	2270	23,800	73·9	8·9
Residue	—	0·25	—	—	—	—	—
Calc. for $C_{12}H_{16}O_2$		—	—	—	—	74·2	9·3

Determinations of absorption spectra were made in alcoholic solution on a Hilger E_3 quartz spectrograph in conjunction with a Spekker photometer, standard methods being used.

We thank Mr. R. P. Merritt for his interest in this investigation of the pyrethrins, and one of us (T. F. W.) is indebted to the Directors of Messrs. Stafford Allen and Sons, Ltd., for facilities and to Mr. J. B. S. Wilson for assistance in the tedious purification of the pyrethrum extracts.

THE UNIVERSITY, MANCHESTER.
STAFFORD ALLEN AND SONS, LTD., LONDON, N.1.

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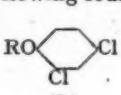
140. *The Halogenation of Phenolic Ethers and Anilides. Part XIII. Arrhenius Activation Energies for Di- and Poly-substituted Aromatic Ethers.*

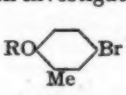
By BRYNMOR JONES.

The kinetic study of the nuclear chlorination of aromatic ethers at temperatures between 15° and 35° has been extended to di- and poly-substituted ethers which contain activating as well as deactivating substituents. In each case there is only one position available for substitution. Analysis of the results on the basis of the equation $k = PZe^{-E/RT}$ shows that the variations in the *P* term are small and within the error of experiment, while the energy of activation varies from 9,900 to 14,350 cals.

A RECENT detailed investigation of the rates of nuclear chlorination of 21 ethers of the type *p*-OR·C_6H_4X at temperatures between 15° and 35° showed that the *P* term of the expression $k = PZe^{-E/RT}$ is constant within the limits of experimental error, while *E* varies from 9,850 to 14,650 cals. (this vol., p. 418). This result confirms the original view, first put forward in 1928, that the observed regularities in the relative influences of substituent groups on the rates of nuclear chlorination of these ethers are simply and adequately accounted for by assuming that each group contributes a characteristic quota to the energy of activation. The results of a limited number of measurements are now recorded for certain di- and poly-substituted aromatic ethers, and the same conclusion is reached. In these series the range of suitable compounds is more restricted, but members of the following four types have been investigated :



(I.)



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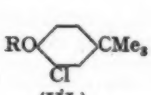
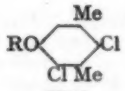


(III.)



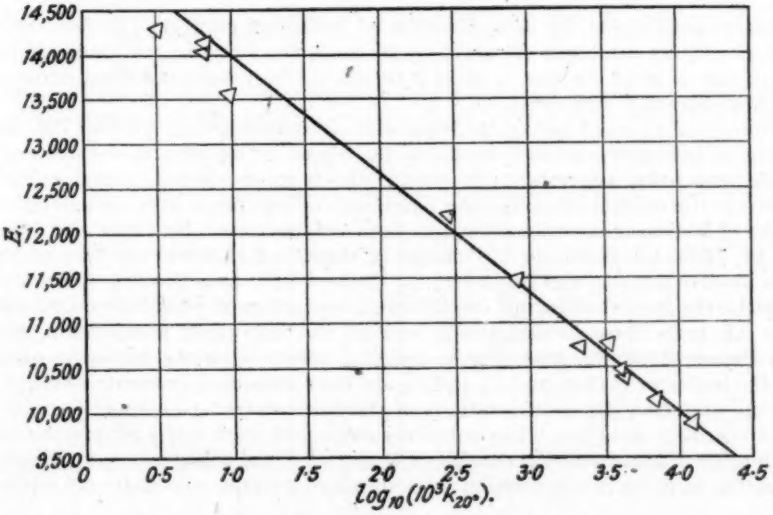
(IV.)

The results are summarised in the table. Where measurements were made at more than two temperatures the values of *E* were obtained by plotting log *k* against $1/T$; in other cases they were calculated from the usual expression. Values of log *PZ* were derived from these values of *E* and the velocity coefficients at 20°.

Velocity coefficients for the chlorination of di- and poly-substituted aromatic ethers in 99% acetic acid.

Type.	R.	$k_{15°}$.	$k_{20°}$.	$k_{30°}$.	$k_{35°}$.	*E* (cals.).	log *PZ*.
IV	Me	9·52	12·50	—	29·1	9,900	8·49
IV	CH_2Ph	—	7·14	—	16·7	10,150	8·43
IV	$CH_2·C_6H_4Cl(p)$	3·19	4·37	—	10·34	10,400	8·40
II	Me	—	4·10	7·45	9·85	10,500	8·46
IV	$CH_2·C_6H_4Cl(m)$	2·45	3·38	6·22	8·44	10,800	8·59
II	CH_2Ph	—	2·18	4·01	5·35	10,750	8·36
IV	$CH_2·CO_2H$	—	0·836	1·60	2·19	11,500	8·50
III	$CH_2·C_6H_4·NO_2(p)$	—	0·291	—	0·811	12,250	8·63
I	$CHMe_2$	—	0·0095	—	0·0296	13,600	8·12
I	CH_2Et	—	0·0067	0·0150	0·0216	14,150	8·39
I	Et	—	0·00636	—	0·0206	14,050	8·29
I	Me	—	0·0031	—	0·0103	14,350	8·20

When $\log_{10}(10^3 k_{20°})$ for each ether is plotted against *E* (see figure), all the points fall on or near the same straight line, of slope $-2·303RT$, as did the ethers of the simpler type *p*-OR C_6H_4X. Hence, although the present



series of measurements are limited to a smaller number of ethers, and in some cases to a narrower range of temperature, than were those for the ethers of the type *p*-OR·C_6H_4X, yet together with these they show clearly that the variations in the *P* term on passing from one series of ethers to another are insignificant in comparison with the variations in the energy of activation.*

There is one further point arising out of these results. In considering the nuclear reactivity of di- and poly-substituted ethers of the above types with those of the simpler type *p*-OR·C_6H_4X, it is reasonable to suppose that the *P* term for the latter includes an additional factor 2 resulting from the presence of two similar vacant

* The variations (of the order of 15%) in the relative directive power of OR groups discussed in Part X (J., 1941, 275) may, as there suggested, indicate small changes in the probability factor, but the relatively wide limits of error necessarily involved in the computation of *P* by the present method of analysis render such small variations quite insignificant.

ortho-positions available for substitution. The existence of such a factor would require that values of log $2k$ rather than of log k for the di- and poly-substituted ethers should fall on the straight line shown in the figure. Inspection shows that, while values of log $2k$ for the four alkyl ethers of dichlorophenol would fall more closely on the line than the values of log k plotted, yet the corresponding values for the other eight ethers would all lie distinctly to the right of the line. It appears, therefore, that the present series of measurements are too restricted in scope to allow of a decision on this point. Evidence of another type for the existence of a purely statistical factor based on the number of positions available for substitution has been discussed previously (J., 1936, 1854).

Experimental.

Materials.—Pure crystalline specimens of several of the ethers were available from earlier investigations (J., 1941, 267). 2-Chloro-4-*tert.*-butylphenol was prepared in excellent yield from *p-tert.*-butylphenol (J., 1941, 363) by Orton and King's method of controlled chlorination, freshly-prepared chloroacetamide being used as the source of chlorine (J., 1911, **99**, 1185; Orton and Bradfield, J., 1927, 993). When all the chlorine had reacted, the acetamide was removed by addition of water, and the 2-chloro-4-*tert.*-butylphenol extracted with ether. The extract was washed with (*a*) aqueous sodium bicarbonate and (*b*) water, dried, and the solvent removed. The residue of 2-chloro-4-*tert.*-butylphenol distilled at 113—115°/8 mm. The p-*nitrobenzyl ether* was crystallised thrice from ethyl alcohol and separated as colourless plates, m. p. 90° (Found: N, 4·7. $C_{17}H_{18}O_3NCl$ requires N, 4·4%). Similarly 2 : 4-dichloro-3 : 5-dimethylphenol was prepared from 2-chloro-5-*m*-xylenol (cf. Part X, J., 1941, 275); 2 : 4-*dichloro*-3 : 5-*dimethylphenoxyacetic acid* after two crystallisations from benzene was recrystallised from acetic acid, from which it separated in colourless prisms, m. p. 146° (Found: Cl, 28·4; equiv., 252. $C_{10}H_{10}O_3Cl_2$ requires Cl, 28·5%; equiv., 249). The acetic acid was purified by distillation from chromic anhydride and acetic anhydride as described by Orton and Bradfield (J., 1927, 983).

Measurements.—The method of determining the velocity coefficients and the precautions taken to ensure accurate values were the same as in Part XII (this vol., p. 418).

The author is indebted to the Chemical Society for a grant.

The University, Sheffield, 10. [*Received, August 26th*, 1942.]

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141. *Automatic Adjustment of Solute Concentration in the "Moving-boundary" Method for the Determination of Transport Numbers.*

By Robert Wright.

The change in concentration of the indicator solution which takes place with the passage of current in the moving-boundary method for the determination of transport numbers has been determined by direct chemical analysis of samples of the solution taken from different parts of the transport apparatus.

The moving-boundary method for the determination of transport numbers has now been carried to a high degree of accuracy, chiefly by American workers (see McInnes and Longsworth, *Chem. Reviews*, 1932, **11**, 171). Although the apparatus required for this method is intricate, the results obtained surpass those of the older Hittorf method in both accuracy and speed.

The method employs solutions of two electrolytes with a common anion, AR and BR, and requires that the less mobile following, or indicator, cation B should at the boundary travel with the same speed as the cation A whose transport number is being determined; in general, this involves a change in concentration of the indicator solution taking place in the neighbourhood of the boundary during the progress of a determination.

This adjustment of indicator concentration has been demonstrated by Cady and Longsworth (*J. Amer. Chem. Soc.*, 1929, **51**, 1656) by observing the change in resistance of the electrolyte as the boundary moved along the tube. A similar method was employed by Drew, Collie, and Hartley (*Trans. Faraday Soc.*, 1934, **30**, 648), who emphasise the irregularities involved by the introduction of subsidiary electrodes into the boundary tube. The results of both these investigations verified the important relationship, first put forward by Kohlrausch (*Ann. Physik*, 1897, **62**, 209), $T_a/T_b = C_a/C_b$, where T_a is the transport number of the leading cation, T_b that of the indicator cation, and C_a and C_b are their respective concentrations at the boundary.

In the present investigation the concentrations of the electrolytes at different parts of the tube were determined by direct chemical analysis. The solutions employed were N/2-hydrochloric acid, followed by a solution of alkali chloride of concentration between N/2 and N/8; the changes in concentration were thus easily determined by titrating samples of the solution with standard sodium carbonate and silver nitrate solutions.

Experimental.

The tube containing the solution was constructed in sections separated from one another by parchment paper. Each section—or cell—consisted of three square pieces of rubber, of 40 mm. edge and 5 mm. thickness, clamped together so as to give a small block 15 mm. thick. Through the centre of each square a circle of 16 mm. diameter was cut, and the middle square of each cell had a slot 5 mm. wide running from the middle of the top edge to the central hole. This slot served for the introduction and withdrawal of solution. The volume of the complete cell (exclusive of the filling slot) was about 3 c.c., thus sufficing for the withdrawal of 2 c.c. of the solution for analysis.

The complete rubber tube of 16 cells with their parchment separators was assembled in a horizontal open-ended wooden trough. At each end of the tube was placed a square of vulcanised fibre, of the same shape and dimensions as the rubber squares. Two 300 c.c. tubulated bottles, with their mouths ground flat, were laid on their sides with the tubulures uppermost and adjusted so that the mouth of each bottle bore against a fibre end-piece of the composite tube, a washer of soft rubber being placed between the bottle mouth and the fibre. The complete assembly of tube and bottles was

firmly clamped together by means of a pair of wooden wedges which were inserted between the base of one bottle and a stop fixed to the baseboard of the trough; the second bottle bore against a similar stop at the other end of the apparatus.

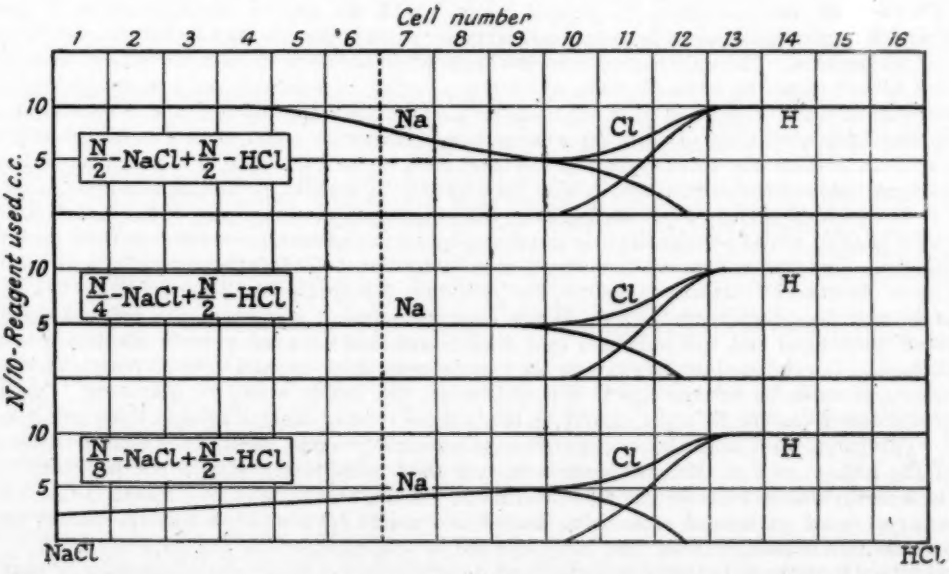
The apparatus being assembled and made watertight by means of the wedges, one bottle and the six cells adjoining it were filled with the alkali chloride solution, the remaining cells and the second bottle with N/2-hydrochloric acid. The liquid in the neck of each cell was now removed by temporarily inserting a glass rod into the cell so that some liquid overflowed, and this surplus was removed by mopping with cotton wool; this clearing of the cell neck was necessary, as the solution in that part of the cell would not be affected by the passage of the current. An amalgamated zinc anode was now placed in the bottle containing the solution of the alkali chloride, and a platinum cathode in the acid solution. A current of 50 milliamps., hand-regulated by means of a series resistance, was passed through the solution for 4 hours. After this passage of 200 milliamp.-hours, 2 c.c. of solution were removed from each cell and titrated first with N/10-sodium carbonate and then with N/10-silver nitrate; from these titrations, which are shown in the table against H and Cl, the concentrations of acid and alkali salt were found. At least two determinations were carried out in each case, the two titres for any one cell being often identical and seldom differing by more than 0·2 c.c.

Anode soltn.*		Cell number. 1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.
N/2-KCl	H	—	—	—	—	—	—	—	—	—	0·4	2·6	8·2	10	10	10	10
	K	10	10	10	9·5	9·0	8·6	7·5	6·9	6·5	5·6	4·3	0·8	—	—	—	—
	Cl	10	10	10	9·5	9·0	8·6	7·5	6·9	6·5	6·0	6·9	9·0	10	10	10	10
N/4-KCl	H	—	—	—	—	—	—	—	—	—	0·5	2·9	8·0	10	10	10	10
	K	5·0	5·0	5·0	5·2	5·5	5·9	6·1	6·4	6·6	6·3	4·3	1·0	—	—	—	—
	Cl	5·0	5·0	5·0	5·2	5·5	5·9	6·1	6·4	6·6	6·8	7·2	9·0	10	10	10	10
N/8-KCl	H	—	—	—	—	—	—	—	—	—	0·6	3·4	7·9	10	10	10	10
	K	2·5	2·7	3·0	3·2	3·5	4·2	4·8	5·5	5·8	5·5	3·8	1·0	—	—	—	—
	Cl	2·5	2·7	3·0	3·2	3·5	4·2	4·8	5·5	5·8	6·1	7·2	8·9	10	10	10	10
0·3N-KCl	H	—	—	—	—	—	—	—	—	—	0·6	3·7	8·5	10	10	10	10
	K	6·0	6·0	6·0	6·0	6·0	6·0	6·0	6·0	6·0	5·6	3·4	0·8	—	—	—	—
	Cl	6·0	6·0	6·0	6·0	6·0	6·0	6·0	6·0	6·0	6·2	7·1	9·3	10	10	10	10
N/2-NaCl	H	—	—	—	—	—	—	—	—	—	0·4	3·1	8·6	10	10	10	10
	Na	10	10	10	10	9·3	8·4	7·2	6·0	5·4	4·6	3·2	0·4	—	—	—	—
	Cl	10	10	10	10	9·3	8·4	7·2	6·0	5·4	5·0	6·3	9·0	10	10	10	10
N/4-NaCl	H	—	—	—	—	—	—	—	—	—	0·3	3·0	8·7	10	10	10	10
	Na	5·0	5·0	5·0	5·0	5·0	5·0	5·0	5·0	5·0	4·6	3·0	0·3	—	—	—	—
	Cl	5·0	5·0	5·0	5·0	5·0	5·0	5·0	5·0	5·0	4·9	6·0	9·0	10	10	10	10
N/8-NaCl	H	—	—	—	—	—	—	—	—	—	0·3	3·0	8·7	10	10	10	10
	Na	2·5	2·5	2·7	2·9	3·4	4·0	4·2	4·4	4·7	4·7	3·0	0·3	—	—	—	—
	Cl	2·5	2·5	2·7	2·9	3·4	4·0	4·2	4·4	4·7	5·0	6·0	9·0	10	10	10	10
N/2-LiCl	H	—	—	—	—	—	—	—	—	—	1·0	4·2	8·0	9·5	10	10	10
	Li	10	10	10	10	9·0	8·1	6·3	5·3	4·3	3·5	1·6	0·4	0·1	—	—	—
	Cl	10	10	10	10	9·0	8·1	6·3	5·3	4·3	4·5	5·8	8·4	9·6	10	10	10
N/4-LiCl	H	—	—	—	—	—	—	—	—	—	0·8	4·4	8·5	10	10	10	10
	Li	5·0	5·0	5·0	5·0	5·0	5·0	4·6	4·2	4·0	3·3	1·6	0·2	—	—	—	—
	Cl	5·0	5·0	5·0	5·0	5·0	5·0	4·6	4·2	4·0	4·1	6·0	8·7	10	10	10	10
N/8-LiCl	H	—	—	—	—	—	—	—	—	—	0·8	4·0	8·4	9·6	10	10	10
	Li	2·5	2·6	2·7	2·9	3·1	3·3	3·5	3·8	4·0	3·4	2·0	0·3	0·2	—	—	—
	Cl	2·5	2·6	2·7	2·9	3·1	3·3	3·5	3·8	4·0	4·2	6·0	8·7	9·8	10	10	10
N/5-LiCl	H	—	—	—	—	—	—	—	—	—	1·0	3·7	7·3	9·0	10	10	10
	Li	4·0	4·0	4·0	4·0	4·0	4·0	4·0	4·0	4·0	3·4	2·0	0·5	0·2	—	—	—
	Cl	4·0	4·0	4·0	4·0	4·0	4·0	4·0	4·0	4·0	4·4	5·7	7·8	9·2	10	10	10

Salt solutions at start. Acid solutions at start.

* The cathode solution in every case was N/2-HCl.

Considering the results for the sodium chloride–acid transference (see fig.) we find that when both solutions are N/2 there is a fall in saline concentration at the neighbourhood of the boundary, but when N/8-sodium chloride is used an



increase in the salt concentration results; with N/4-salt and N/2-acid the concentration of the salt solution remains constant at the boundary. With potassium chloride the concentration of this unchanging solution is 0·3N, and with

lithium chloride 0·2N. These figures represent approximately the concentrations of the salt solutions which do not require adjustment at the boundary in contact with N/2-hydrochloric acid, and therefore should agree with the equation $T_a/T_b = C_a/C_b$. Now the values of the cation transport numbers for the different solutions are: 0·5N-HCl, 0·840; 0·3N-KCl, 0·493; 0·2N-NaCl, 0·385; 0·2N-LiCl, 0·304 (International Critical Tables), and hence we have

	T_a/T_b.	C_a/C_b.		T_a/T_b.	C_a/C_b.		T_a/T_b.	C_a/C_b.
H/K	1·70	1·66	H/Na	2·18	2·00	H/Li	2·76	2·50

The agreement is only approximate, as the experimental method does not indicate with sufficient exactness the concentration of indicator solution in equilibrium at the boundary.

The measurements were not, however, undertaken for the determination of transport numbers, but to observe the changes in concentration at different parts of the tube produced by the passage of the current. In contrast to the methods of Cady and Longsworth and of Drew, Collie, and Hartley, the present method indicates the concentrations existing at different parts of the tube at the same instant, and not the change in concentration at the same part of the tube at different times due to the passage of the boundary.

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142. *Preparation of Certain 3-Substituted Indoles.*

By (MRS.) RITA H. CORNFORTH and SIR ROBERT ROBINSON.

Indole and indole-2-carboxylic acid are converted by methanolic sodium methoxide at 210—220° into skatole, which may be conveniently prepared in this way.

The scope of these methods of 3-alkylation has been investigated. The carboxylic acid may be used with aliphatic primary alcohols, with benzyl alcohol, and γ-phenylpropyl alcohol, and their sodio-derivatives. β-Phenylethyl alcohol gave a complex mixture from which no pure substance could be isolated and β-ethoxyethyl alcohol and ethylene glycol gave 3-ethylindole. No tryptamine or ketotetrahydro-carboline was obtained from indole-2-carboxylic acid, ethanolamine, and its sodio-derivative under the usual conditions.

Indole-2-carboxylic acid could not be alkylated by means of secondary alcohols and their sodio-derivatives. On the other hand, indole could be converted into 3-*iso*propylindole, and 7-methylindole was transformed into 3-cyclo*hexyl*-7-*methylindole*.

SKATOLE finds application in the perfumery industry, but none of the numerous methods hitherto available for its preparation is satisfactory from the technical point of view.

Having improved Reissert's synthesis of indole-2-carboxylic acid (*Ber.*, 1897, **30**, 1030) and the decarboxylation of the latter with formation of indole, it occurred to us that skatole (or its carboxylic acid) might be obtainable by a process of direct methylation of these intermediates.

The *C*-methylation of ethyl *o*-nitrophenylpyruvate (Kermack, Perkin, and Robinson, J., 1921, **119**, 1609) was found unpromising on account of the formation of by-products.

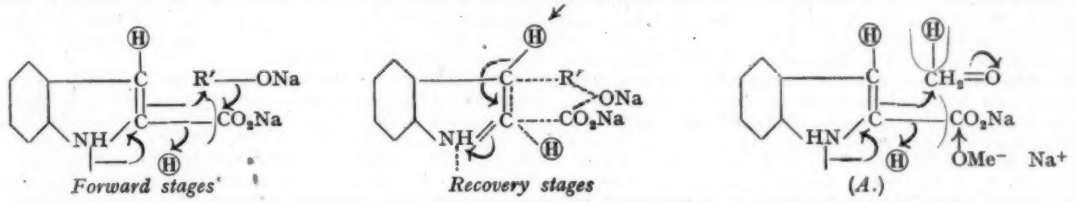
When indole-2-carboxylic acid was heated under pressure with methanolic hydrogen chloride, the products were the methyl ester and tar.

In the pyrrole series much use has been made of methylation by means of hot methanolic sodium methoxide (cf., *e.g.*, Fischer and Bartholomäus, *Z. physiol. Chem.*, 1912, **80**, 10, for the conversion of hæmopyrrolecarboxylic acid into phyllopyrrolecarboxylic acid) whereby methyl groups may be introduced in the 2- or the 3-position of the nucleus. The only examples of the application of this method in the indole series are recorded by Oddo and Alberti (*Gazzetta*, 1933, **63**, 236), who made a variety of 3-substituted 2-methylindoles in this way. These authors state that indole itself does not undergo the reaction (methylation) and is recovered unchanged, but do not record the conditions of their experiment in specific terms. Our work was fortunately carried out before this communication was noted and under the conditions we used the yield of skatole from indole was 71%.

We find that indole-2-carboxylic acid is also converted into skatole by methanolic sodium methoxide at 210—220°. The yield is slightly lower in this case, but if indole is made by way of the 2-carboxylic acid, the overall yield of skatole would be considerably improved by taking advantage of the combined methylation and decarboxylation. For this reason we have paid more attention to indole-2-carboxylic acid as the starting point and have obtained in this way: skatole, 3-ethylindole, 3-*propylindole*, 3-n-*butylindole*, 3-*n*-heptylindole, 3-*benzylindole*, and 3-γ-*phenylpropylindole*. When *iso*propyl alcohol was used, the indole-2-carboxylic acid was recovered unchanged and this indicates that decarboxylation does not precede alkylation in the case of primary alcohols. For if decarboxylation were the first process, there appears to be no reason why it should not occur in *iso*propyl-alcoholic solution, and, if it did occur, the indole would be alkylated. Apparently the 3-substituted indole-2-carboxylic acids should be much more readily decarboxylated than indole-2-carboxylic acid itself. This is not what would be anticipated on theoretical grounds, because the elimination is a cationoid reaction of the sodium salt of the carboxylic acid and alkyl substitution should not facilitate it. A small specimen of 3-methylindole-2-carboxylic acid (Kermack, Perkin, and Robinson, J., 1921, **1634**) was available and this was recovered unchanged after being heated in a sealed tube with methanolic sodium methoxide at 210°; the production of skatole could only be recognised by smell and by the Ehrlich reaction.

An alternative hypothesis is that alkylation and decarboxylation occur simultaneously or nearly so. On this basis one would expect the product to be a 2-substituted indole produced by displacement, and the formation of the 3-derivative can only be explained by the assumption of intramolecular electronic displacements (p. 681),

which as usual are assumed to alternate * until the processes are completed. This is a simplification based on an admittedly erroneous representation of the function of R'ONa. It is presented merely to illustrate the possibility of virtual migration. Probably the aldehyde or ketone corresponding to the alcohol is liberated in a reactive form from the alkoxy-ion and the product of condensation of this with the indole derivative is



Forward stages *Recovery stages* (*A.*)

later reduced (cf. the following paper). Thus in the case of methylation the first hypothetical stages can be expressed more accurately by scheme (*A*). Although it is possible to formulate such a process, the elimination and substitution reactions are seen to be distinct and do not collaborate in so far as the displacements are concerned. There may be a general activation of the molecule which exerts a trigger action. A decision between the two hypotheses (*a*) alkylation, followed by decarboxylation, and (*b*) alkylation with virtually simultaneous decarboxylation, cannot yet be made. Included in (*b*) would be the possibility that an intermediate in the process is especially readily decarboxylated.

The methylation of indole itself to skatole shows that there is no tendency for the 2-position to be attacked. Similarly, 7-methylindole afforded 3 : 7-dimethylindole.

Indole, sodium *iso*propoxide and *iso*propyl alcohol reacted with formation of 3-*iso*propylindole and 3-cyclo*hexyl*-7-*methylindole* was prepared from 7-methylindole, *cyclo*hexanol, and its sodio-derivative. Indole was recovered unchanged after being heated at 210—220° with *tert.*-butyl alcohol and its sodio-derivative.

Experimental.

Indole-2-carboxylic Acid.—*o*-Nitrophenylpyruvic acid was prepared according to Mayer and Balle (*Annalen*, 1914, **403**, 1188). Sodium hydrosulphite (about 230 g.; the amount needed varies with quality) was added to a cold, stirred solution of *o*-nitrophenylpyruvic acid (90 g.) in aqueous sodium hydroxide (20 g. in 700 c.c.) until a test portion no longer became red on the addition of excess of sodium hydroxide; the temperature rose to 40—45°. The cooled solution was acidified with hydrochloric acid (160 c.c., *d* 1·16) and then heated on the steam-bath to expel sulphur dioxide. The product (45 g. or 64·9%; m. p. 200—202°) was collected by means of ether and so separated from insoluble solid material.

General Method.—Except when stated otherwise, the indole, or derivative, (10 g.) was heated in an autoclave with the alcoholic sodium alkyloxide (from 12 g. of sodium in 150 c.c.) for 12 hours at 210—220°. Where variations are mentioned, the other conditions remained unaltered.

Skatole.—(a) *From indole-2-carboxylic acid.* The solvent was removed by distillation and steam-distillation. Continued steam-distillation gave 5·2 g. (63%) of skatole, m. p. 93° alone or mixed with an authentic specimen. The Ehrlich reaction was identical with that shown by an authentic specimen.

(b) *From indole.* The product was isolated in the same way (8 g., 71%), m. p. 93°.

3-*Ethylindole.*—Indole-2-carboxylic acid and ethyl alcohol (210 c.c.) were used. The mixture was steam-distilled, and the distillate collected after removal of the alcohol. It was saturated with sodium chloride; the product, isolated by means of ether, had b. p. 150—156°/20 mm. and crystallised in large plates, m. p. 37° (5·6 g., 62%) (Found : C, 82·6; H, 7·6; N, 9·5. Calc. for $C_{10}H_{11}N$: C, 82·8; H, 7·6; N, 9·6%). The Ehrlich reaction (2 g. of *p*-dimethylaminobenzaldehyde in 100 c.c. of alcohol and 25 c.c. of hydrochloric acid, *d* 1·16) was a blood-red coloration in the cold and reddish-purple on boiling. The colours may be alternated by heating and cooling. On continued heating the colour becomes bluer and duller.

The picrate crystallised from benzene–light petroleum (b. p. 60—80°) in red needles, m. p. 121°, and, in agreement with von Braun and Bayer (*Ber.*, 1925, **58**, 391), the same m. p. was found for the picrate of the cyclisation product of *n*-butaldehydephenylhydrazone by means of zinc chloride; a mixture of the specimens had m. p. 121° (Found : N, 14·8%).

On the other hand, Pictet and Duparc (*Ber.*, 1887, **20**, 3416) (reaction of aniline with lactic acid in the presence of zinc chloride) give m. p. 143°; Oddo (*Gazzetta*, 1911, **41**, 232) (ethyl iodide on indolymagnesium iodide) gives m. p. 144·5°; Korczynski, Brydowna, and Kiersck (*ibid.*, 1926, **56**, 905) (Fischer method using nickel chloride) give m. p. 143—144°; Alberti (*ibid.*, 1937, **67**, 238) (sodium ethoxide on 3-acetylindole) gives m. p. 143—144°; all for the picrate of 3-ethylindole. A specimen was prepared by the addition of saturated alcoholic picric acid to a slight excess of pure 3-ethylindole The red needles were collected, washed with light petroleum, and dried in a vacuum, m. p. 120—121° (Found : C, 51·1; H, 4·0. $C_{10}H_{11}N,C_6H_3O_7N_3$ requires C, 51·3; H, 3·7; N, 15·0%). This experiment was performed so as to avoid dissociation by recrystallisation and in order to use a different solvent. It would appear that the substance may exist in two modifications, but we have only encountered that of the lower m. p.

3-n-*Propylindole.*—This *substance* is mentioned, without any details, in G.P. 38,784 and the same applies to 3-*n*-butyl- and 3-benzyl-indoles. It was obtained from indole-2-carboxylic acid and propyl alcohol (250 c.c.). The product, isolated as in the preceding case, was an almost colourless oil (6·3 g., 64%), b. p. 162—164°/20 mm. (Found : C, 82·8; H, 8·3; N, 8·5. $C_{11}H_{13}N$ requires C, 83·0; H, 8·2; N, 8·8%). The picrate crystallised in red needles, m. p. 113—114°, from benzene–light petroleum (b. p. 60—80°). The Ehrlich reaction was the same as that shown by 3-ethylindole.

3-iso*Propylindole.*—Under the usual conditions with *iso*propyl alcohol, indole-2-carboxylic acid was recovered unchanged. Indole (5 g.), *iso*propyl alcohol (130 c.c.), and sodium (6 g.) were used. The product was a colourless oil

* I do not concur with Ingold and Hughes (J., 1941, 608), for whom chronology in electronic displacements has ceased to have any meaning. In particular, the argument derived from the " uncertainty " principle is not valid, because it refers to a time-scale altogether finer graded than that applicable to displacements represented by the symbols $\longrightarrow$ and $\curvearrowright$. These are assumed to be tangible processes and the conditions resulting from them exist for a definite, though doubtless often very small, period of time. They are the statistical averages of a number of single displacements, to each of which the uncertainty principle can properly be applied. R. R.

(4·3 g., 63%), b. p. 155—160°/20 mm. (Found: C, 82·8; H, 8·4; N, 8·7%). The picrate crystallised in red needles, m. p. 102—103°, and the Ehrlich reaction was normal, but the blood-red colour made its appearance very much more slowly than with 3-propylindole. For comparison 5 c.c. of the reagent were added to one drop of the indole derivative. The substance has previously been prepared from *iso*valeraldehydephenylhydrazone (Trenkler, *Annalen*, 1888, **248**, 106) and the m. p. 98—99° assigned to the picrate.

3-n-*Butylindole*.—Indole-2-carboxylic acid and *n*-butyl alcohol (250 c.c.) were used. The *product* was a colourless oil (6·6 g., 62%) (Found: C, 82·8; H, 8·7; N, 8·1. $C_{12}H_{15}N$ requires C, 83·2; H, 8·7; N, 8·1%). The picrate crystallised from benzene–light petroleum (b. p. 60—80°) in red needles, m. p. 114°, and the Erhlich reaction was normal; there was no perceptible slowness of appearance of the coloration as compared with 3-ethylindole.

3-n-*Heptylindole*.—Indole-2-carboxylic acid and *n*-heptyl alcohol (210 c.c.) were used. The isolated neutral products on distillation afforded unchanged heptyl alcohol (120 g.), a fraction (12 g.), b. p. 165—185°/15 mm., which solidified to a wax (cf. Guerbet, *Compt. rend.*, 1901, **132**, 207, for the products of condensation of heptyl alcohol in the presence of sodium heptoxide at 220°), a fraction (A) (14 g.), b. p. 145—175°/0·3 mm., a fraction, b. p. 175—195°/0·3 mm., and residue. (A) on redistillation gave 6 g., b. p. 155—165°, which solidified. The substance, after two crystallisations from light petroleum (b. p. 60—80°), was obtained in colourless needles, m. p. 60° (Found: C, 83·3; H, 9·8; N, 6·8. Calc. for $C_{15}H_{21}N$: C, 83·7; H, 9·8; N, 6·5%). The Erhlich reaction was first blood-red and then bluish cherry-red in the cold; on heating, the colour became deeper and similar to that obtained in the preceding cases. The orange picrate dissociated when an attempt was made to crystallise it. 3-*n*-Heptylindole has been made by Korczynski *et al.* (*loc. cit.*) by the Fischer reaction using nickel chloride as catalyst. It is described as a reddish oil, b. p. 179—182°/3 mm.

3-*Benzylindole*.—Indole-2-carboxylic acid and benzyl alcohol (200 c.c.) were used. Steam-distillation was continued until the oil came over slowly and partly crystallised. The neutral oil remaining in the flask was isolated by means of ether and then solidified. The *substance* crystallised from light petroleum (b. p. 80—100°) in colourless, prismatic needles (8·5 g.; 66%), m. p. 103°. Recrystallisation from the same solvent and then from aqueous alcohol raised the m. p. to 111° (Found: C, 87·0; H, 6·5; N, 6·7. $C_{15}H_{13}N$ requires C, 87·0; H, 6·3; N, 6·6%). With the Ehrlich reagent the coloration appeared very slowly in the cold; on heating, the purplish colour was a shade bluer than with 3-ethylindole.

The picrate crystallised from benzene–light petroleum (b. p. 60—80°) in red needles, m. p. 115°. About 40 g. of benzoic acid were produced in the formation process and the odour of benzaldehyde was observed.

3-*γ-Phenylpropylindole*.—Indole-2-carboxylic acid and γ-phenylpropyl alcohol (180 c.c.) were used (time, 14 hours). The neutral products were isolated by means of ether and on distillation gave unchanged phenylpropyl alcohol (60 g.), 35 g. of material, b. p. 160—175°/0·2 mm., and 3·4 g., b. p. 175—180°/0·2 mm. The last solidified and after three recrystallisations from light petroleum (b. p. 40—60° and later b. p. 60—80°), the *substance* was obtained in colourless needles, m. p. 73° (Found: C, 86·5; H, 7·4; N, 5·9. $C_{17}H_{17}N$ requires C, 86·8; H, 7·2; N, 6·0%). A further 3 g. was obtained by refractionation of the large second fraction. The Ehrlich reaction was normal, but when the hot solution was cooled the colour faded to a bluish-red and not to the original blood-red. The picrate separated from benzene–light petroleum (b. p. 60—80°) in dark red, flat needles, m. p. 116°. β-Phenylpropionic acid (30 g.) was isolated from the aqueous alkaline solution and other products were formed but not further investigated.

3 : 7-*Dimethylindole*.—This was prepared from 7-methylindole, and the product (8 g.; 75%) isolated as in the case of skatole. It crystallised from light petroleum (b. p. 40—60°) in colourless plates, m. p. 56° (Found: C, 82·7; H, 7·7; N, 9·6. Calc. for $C_{10}H_{11}N$: C, 82·8; H, 7·6; N, 9·6%). The Ehrlich reaction was a cherry-red coloration in the cold, greatly intensified on heating, and the picrate crystallised from light petroleum (b. p. 60—80°) in red needles, m. p. 164°. Mendlik and Wibaut (*Rec. Trav. chim.*, 1911, **50**, 109) prepared the substance by the Fischer reaction but describe it as an oil, picrate, m. p. 142—143°.

3-cyclo*Hexyl*-7-*methylindole*.—7-Methylindole (5 g.), sodium (6 g.), and *cyclo*hexanol (200 c.c.) were used. The mixture was steam-distilled to remove *cyclo*hexanol; on cooling, the residual oil in the flask partly crystallised. It was taken up in methyl alcohol; on keeping, 3-cyclo*hexyl*-7-*methylindole* separated in colourless, rhombic plates (5·6 g.; 82%), m. p. 115° (Found: C, 84·7; H, 9·2; N, 6·6. $C_{15}H_{19}N$ requires C, 84·5; H, 8·9; N, 6·6%). The picrate dissociated, even in non-hydroxylic solvents. The Ehrlich reaction was a brownish-red coloration in the cold that made its appearance slowly; on heating, the colour changed to deep reddish-purple.

Miscellaneous Reactions.—Indole-2-carboxylic acid and ethylene glycol (200 c.c.) afforded 4 g. of 3-ethylindole. With the same quantity of β-ethoxyethanol the yield of 3-ethylindole was 5·9 g. Similarly, ethanolamine (200 c.c.) gave rise to the formation of 1·4 g. of basic material, b. p. 180—200°/0·67 mm., but this could not be purified. No better result was obtained with β-diethylaminoethanol. Benzylidenebis-2-methylindole and methyl alcohol (10 hours at 220—230°) furnished 2 : 3-dimethylindole (5·5 g.), separated by steam-distillation. The neutral substances remaining in the flask were isolated by means of ether and after crystallisation from light petroleum (b. p. 60—80°) and from alcohol, furnished stout, colourless prisms, m. p. 119—120° (yield, about 1 g.) (Found: N, 6·6. Calc. for $C_{16}H_{15}N$: N, 6·3%). The substance is evidently 3-benzyl-2-methylindole (Kuroda, *J. Pharm. Soc. Japan*, 1923, **493**, 131; Hushino, *Annalen*, 1932, **500**, 40). The Ehrlich reaction was negative in the cold; on heating, the solution became brownish-green and then dichroic (red and bluish-green); on cooling, the colour faded to pale yellowish-brown. The yield of 2 : 3-dimethylindole was greater than that which could have resulted from a simple fission into benzylmethylindole and methylindole. Therefore both indole nuclei must have been a source of this substance. In confirmation the yield of benzylmethylindole was low.

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Dyson Perrins Laboratory, Oxford University. [*Received, August 10th*, 1942.]

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143. *Nuclear Methylation of Phenols by Means of Methanolic Sodium Methoxide.*

By John W. Cornforth, (Mrs.) Rita H. Cornforth, and Sir Robert Robinson.

The *C*-methylation of substituted pyrroles by means of sodium methoxide is a useful synthetic reaction which has not hitherto been applied in other series. It is now shown that reactive phenols such as β-naphthol and resorcinol can be methylated under similar conditions. The yield is improved if the phenol is first converted into a methylene-bis-derivative or into a *N*-piperidylmethyl derivative.

The theory of the process is discussed.

If the nuclear methylation of pyrrole derivatives (cf. Fischer-Orth, " Die Chemie des Pyrrols," Leipzig, 1934, I, 33, 287) is regarded as a straightforward interaction with sodium methoxide, it appears anomalous from the

electrochemical point of view because the pyrrole nucleus is decidedly anionoid in polar character and sodium methoxide is an anionoid reagent. Fission into Me^+, O^{--}, and Na^+, which might explain the result, appears highly improbable.

If the pyrrole is assumed to function as an anionoid reagent in the reaction, a natural deduction is that *C*-methylation should succeed with other strongly anionoid substances such as the aromatic tertiary amines and phenols. The latter class was selected for study in the first place because the phenoxide ion is highly reactive and the products in some instances would be useful intermediates for syntheses in progress in the laboratory. It was found that phenol, catechol, quinol and α-naphthol were recoverable unchanged after treatment with methanolic sodium methoxide at 220°.

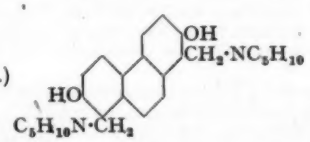
β-Naphthol was partly converted under similar conditions into 1-methyl-2-naphthol and both resorcinol and phloroglucinol afforded dihydroxymesitylene; this reduction of phloroglucinol is significant. Pyrogallol gave a complex mixture of volatile products.

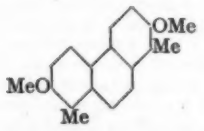
2 : 2′-Dihydroxydi-α-naphthylmethane furnished 1-methyl-2-naphthol in 75% yield, reckoning both nuclei as possible sources of the product. This shows that the nascent β-naphthol produced by the reduction of the methylene derivative is much more effectively methylated than ordinary β-naphthol.

A mixture of methylenedinaphthol (10%) and β-naphthol showed no improvement over the result with the naphthol alone. Hence it is unlikely that the methylenedinaphthol reacts with sodium methoxide so as to give 2 mols. of 1-methyl-2-naphthol and formaldehyde, and in any case such formaldehyde could not long survive under the conditions of the experiment. Thus formaldehyde in small concentration cannot be postulated as a catalyst in a cycle of operations. If it is an intermediate, it must be continuously produced, a portion becoming effective and a portion oxidised and polymerised.

The view that methylenedinaphthol is reduced to methylnaphthol and naphthol is confirmed by the behaviour of benzylidenedi-β-naphthol, which was converted into 1-benzyl-2-naphthol, methylnaphthol and naphthol. 1-Piperidino-2-naphthol is similarly reduced to 1-methyl-2-naphthol and analogously 4-methyl-1-naphthol may be obtained by this modification of the method. Again 2 : 7-*dihydroxy*-1 : 8-*bispiperidinomethylphenanthrene* (I) was reduced by methanolic sodium methoxide to a product, isolated as the *dimethyl ether*, probably (II).

(I.)





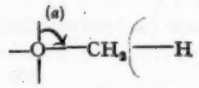
(II.)

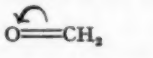
Caldwell and Thompson (*J. Amer. Chem. Soc.*, **1939**, **61**, 765) showed that a piperidinomethylxylenol could be hydrogenated to a trimethylphenol at 165° in the presence of copper chromite. There are several further examples in the literature of the reduction of substituted benzylamine salts to toluene or its derivatives (cf. Emde, *Arch. Pharm.*, **1909**, **247**, 369; *Ber.*, **1911**, **44**, 3224).

In all the processes sodium formate was produced whether methylation occurred or not.

Our view of the mechanism of the reaction is that activated formaldehyde is generated by decomposition of methoxyl ion (A) in presence of a reducible substance. If the negative, reducing hydrogen is detached

(A.)





(B.)

before the process (*a*) becomes a complete transfer of the unshared electrons to covalency, formaldehyde is available in a form strongly cationoid at the carbon atom (B). This will react at once with phenoxide ions to give an arylcarbinol or diarylmethane, which, as independent experiment shows, can be reduced to arylmethane. After the oxygen in the closed system is exhausted, the reducible substances that may be present are the phenol and its transformation products, arylcarbinol and diarylmethane, formaldehyde and its condensation products, sodium formate and methyl alcohol. In addition, hydrogen may be liberated. An analysis of the gaseous products has not yet been carried out, but is desirable, for it may throw light on the details of the mechanism.

We have also considered the possibility that sodium formate may be a formylating agent or that an equilibrium may exist between sodium formate–methyl alcohol and formaldehyde–sodium methoxide. These suggestions are modifications of the general hypothesis and further evidence is necessary before they can be dismissed. The common ground is that sodium methoxide is not itself the methylating agent but that oxidation is a preliminary. The oxidation product then condenses with the phenol and reduction is the final stage.

Experimental.

The phenolic substance (10 g.) was heated in an autoclave at 220°, during the times stated below, with a solution of sodium methoxide (12 g. of sodium) in methanol (150 c.c.).

Resorcinol (10 hours).—The solution was acidified, steam-distilled, clarified with charcoal, and concentrated to 100 c.c. under diminished pressure. On cooling and keeping, light yellow crystals (3·5 g.) were deposited. Purified by sublimation, or crystallisation from benzene, the substance formed flattened, pointed, colourless needles, m. p. 151° (Found: C, 70·7; H, 8·0. Calc. for $C_9H_{12}O_2$: C, 71·1; H, 7·9%). The m. p. and analysis indicate that the substance is 2 : 4 : 6-trimethylresorcinol (dihydroxymesitylene, mesorcinol) (Knecht, *Ber.*, 1882, **15**, 1377). The b. p., reactions

with ferric chloride, lead acetate, silver nitrate and Fehling's solution, and the fluorescein test also corresponded with the description by Knecht.

By ether extraction of the residue, formic acid and a small quantity of an acid forming slender needles from water, m. p. 196° (decomp.), were isolated. This acid gives a bluish-violet ferric reaction and is probably a *C*-methyl- or *C*-dimethyl-β-resorcylic acid, but the amount obtained was insufficient for full investigation.

Phloroglucinol (9 hours).—Worked up as above, only a little tar separated. The solution was repeatedly extracted with ethyl acetate; the residue after removal of the solvent crystallised and was drained on a porous tile (2·5 g.). The material was freed from acidic substances by solution in ether and washing with aqueous sodium bicarbonate. The recovered mesorcinol crystallised from water in needles, m. p. 151° alone or mixed with the specimen from resorcinol.

β-Naphthol (11 hours).—The solvent was steam-distilled, and the solution acidified. When cold the precipitate was collected and heated for 2 hours on the steam-bath with water (50 c.c.), formaldehyde (6 c.c. of 40%), and potassium hydroxide (12 g.), whereby unchanged β-naphthol was converted into the sparingly soluble methylenedinaphthol. The recovered naphthols were repeatedly extracted with boiling water, from which 1-methyl-2-naphthol crystallised in long needles (1·8 g.), m. p. 109—111° (Found: C, 83·4; H, 6·6. Calc. for $C_{11}H_{10}O$: C, 83·6; H, 6·3%). The m. p. was not depressed by an authentic specimen. When the reaction mixture was heated for 22 hours, the yield rose to 3·2 g. β-Naphthol (9 g.) and methylenedinaphthol (1 g.) (10 hours) gave 2·0 g. of methylnaphthol.

Methylenedinaphthol (11 hours).—In this case the condensation of the product with formaldehyde was omitted (needles, m. p. 108—111°; yield, 7 g. and 1 g. more from mother-liquors). Judged by the chloroform–alcoholic sodium hydroxide test, this material contained only a trace of β-naphthol. Assuming quantitative reductive fission to methylnaphthol and naphthol, the latter has furnished about twice as much methylnaphthol as in the experiment starting with preformed β-naphthol.

This method of preparation of methylnaphthol is probably the best now available. On a larger scale, methylenedinaphthol (50 g.), sodium (23 g.), and methyl alcohol (300 c.c.) were heated in a revolving autoclave at 210—220° for 7 hours. The crude product was almost free from β-naphthol and on methylation (35 c.c. of methyl sulphate and 150 c.c. of 10% sodium hydroxide solution) afforded 40 g. of 2-methoxy-1-methylnaphthalene, b. p. 150—155°/10 mm. After one crystallisation from alcohol, the colourless needles had m. p. 41—42°.

Benzylidenedi-β-naphthol (10 hours).—The 1-benzyl-2-naphthol was separated from a mixture of naphthol and methylnaphthol by fractionation in a high vacuum. It crystallised from light petroleum (b. p. 60—80°) in colourless prisms, m. p. 111—112°, depressed to 85—95° by admixture with 1-methyl-2-naphthol (cf. Claisen, *Z. angew. Chem.*, 1923, **56**, 478). The mixture (m. p. 80—95°) of β-naphthol and 1-methyl-2-naphthol constituted th major product; it was treated with formaldehyde in the usual way and methylenedinaphthol and methylnaphthol w re separated and identified.

1-*Piperidinomethyl-2-naphthol* (6 hours).—The mixture was diluted and acidified, and the product crystallised from water. The yield of 1-methyl-2-naphthol was 4·6 g. (70%) and β-naphthol was absent in this case. Similarly, 4-piperidino-1-naphthol (5 hours) afforded 4-methyl-1-naphthol (4 g.); needles, m. p. 84—85°, after two crystallisations from light petroleum. The properties of the substance were in agreement with the description by Lesser (*Annalen*, 1914, **402**, 8), who prepared it from 4-amino-1-methylnaphthalene.

2 : 7-*Dihydroxy*-1 : 8-*bispiperidinomethylphenanthrene* (I).—A solution of 2 : 7-dihydroxyphenanthrene (5 g.) in alcohol (50 c.c.), piperidine (4·1 g.), and aqueous formaldehyde (4 g. of 36·7%) was kept for 12 hours. The solid (8·5 g.) crystallised from ethyl acetate in colourless leaflets, m. p. 219—220° (Found: C, 77·2; H, 7·8; N, 6·6. $C_{26}H_{32}O_2N_2$ requires C, 77·2; H, 7·9; N, 6·9%).

2 : 7-*Dimethoxy*-1 : 8-*dimethylphenanthrene* (II).—The above crude piperidinomethyl compound (5 g.) was reduced as usual (sodium, 10 g.; methanol, 150 c.c.; 6 hours' heating at 200°). The crude phenolic product (2·7 g.) was isolated by means of ether after acidification and at once methylated by treatment with methyl sulphate and sodium hydroxide solution. The resulting dimethyl ether was purified by sublimation at 250°/10 mm. (1·5 g.) and by several crystallisations from benzene, and then from xylene, and obtained in foliated, colourless needles, m. p. 256—257° (Found: C, 81·2; H, 6·8. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%).

Hydrogenation of the dihydroxybispiperidinomethylphenanthrene gave a mixture of products from which no individual substance could be separated. Analysis indicated that octahydro-derivatives of dihydroxydimethylphenanthrene predominated.

The authors thank the Royal Commissioners of the Exhibition of 1851 for Overseas Scholarships awarded to two of them.

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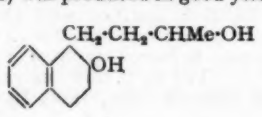
144. *Experiments on the Synthesis of Substances related to the Sterols Part XL.* (A) *The Preparation of 2 : 7-Dihydroxyphenanthrene and Certain Derivatives.* (B) *Further Observations on the Reduction of 1-γ-Ketobutyl-2-naphthol.*

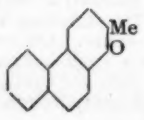
By J. W. CORNFORTH and SIR ROBERT ROBINSON.

This interim report concerns two related topics in that the experiments with β-naphthol furnish a model for similar transformations of 2 : 7-dihydroxyphenanthrene or its monomethyl ether.

(A) A very satisfactory method of preparation of 2 : 7-dihydroxyphenanthrene and its methyl ethers has been devised, based on the synthesis of 2 : 3 : 6 : 7-tetra-acetoxydihydrophenanthrene from 3 : 4 : 3′ : 4′-tetramethoxydibenzyl by Erdtman (*Annalen*, 1933, **505**, 195). As a result this substance and its derivatives become readily accessible and a number of interesting developments are contemplated.

(B) (Compare McQuillin and Robinson, J., 1941, 586.) Pressure hydrogenation of 1-γ-ketobutyl-2-naphthol in the presence of copper chromite furnished the glycol (I), but satisfactory conditions for the oxidation of this substance to the desired diketone have not yet been found. When Raney nickel was used as the catalyst, the fully reduced chroman (II) was produced in good yield.

(I.) 



(II.)

(A) 2 : 7-DIHYDROXYPHENANTHRENE (III, R = R′ = H) was first obtained by Fieser (*J. Amer. Chem. Soc.*, 1929, **51**, 2471) by alkali fusion of the corresponding disulphonic acid, isolated from a mixture produced by the sulphonation of phenanthrene-2-sulphonic acid. In an attempt to find a better procedure, Rapson and Robinson (J., 1935, 1533) applied the Pschorr synthesis, starting with 6-nitro-3-methoxybenzaldehyde and *m*-methoxyphenylacetic acid. 2 : 7-Dimethoxyphenanthrene was obtained in this way, but the major product of the ring-closure stage was 2 : 5-dimethoxyphenanthrene-9-carboxylic acid.

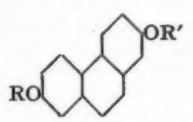
Of the two methods introduced by Erdtman (*loc. cit.*), that depending on a cyclisation by the Ullmann reaction was the more suitable for the purpose in view.

3 : 3′-Dimethoxydibenzyl had been prepared by Späth as a by-product (*Monatsh.*, 1913, **34**, 1999). It was obtainable from 3 : 3′-dimethoxybenzoin (Schönberg and Malchow, *Ber.*, 1922, **55**, 3746) by reduction according to Clemmensen and catalytic reduction of the product, which was found to be mixed with 3 : 3′-dimethoxystilbene. At this stage Erdtman's first method was tried; 3 : 3′-*dihydroxydibenzyl*, prepared by demethylation of its dimethyl ether, gave yellow resins on oxidation with ferric chloride and nothing definite could be isolated from them.

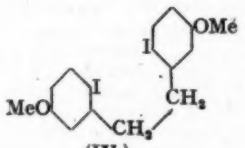
The iodination of 3 : 3′-dimethoxydibenzyl by means of iodine and mercuric acetate in acetic acid solution gave an almost theoretical yield of 6 : 6′-*di-iodo*-3 : 3′-*dimethoxydibenzyl* (IV) and cyclisation by means of copper bronze afforded a 70% yield of 2 : 7-*dimethoxy*-9 : 10-*dihydrophenanthrene*. Under some conditions dehydrogenation to 2 : 7-dimethoxyphenanthrene (III, R = R′ = Me) also occurred but this could be accomplished in any case by heating the dihydro-compound with sulphur.

Improvement of the preparation of dimethoxydibenzyl was found possible by a combination of excellent methods already described.

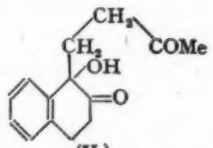
Following Woodward (*J. Amer. Chem. Soc.*, 1940, **62**, 1478), *m*-methoxybenzyl alcohol was obtained in 90% overall yield from *m*-hydroxybenzaldehyde. It was converted into its chloride in 91% yield (cf. Rapson and Robinson, *loc. cit.*, p. 1537) and then into 3 : 3′-dimethoxydibenzyl in 89% yield by an adaptation of the method of Michaelenko and Sassypkina (*J. Russ. Phys. Chem. Soc.*, 1921, **53**, 343).



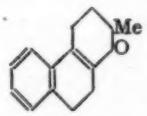
(III.)



(IV.)



(V.)



(VI.)

Demethylation of 2 : 7-dimethoxyphenanthrene is facile and conditions of methylation have been worked out which afford the dimethyl ether and 2-*hydroxy*-7-*methoxyphenanthrene* (III, R = H, R′ = Me) in about equal amount with little loss. This is an improvement on an earlier process in which the monobenzoate was prepared, methylated and hydrolysed. An indication has been obtained that this monomethyl ether can be γ-ketobutylated but the 2-hydroxyphenanthrenes are not analogous to β-naphthol in all respects. For instance, 2 : 7-dihydroxyphenanthrene is not convertible into its methyl ethers by the action of methyl-alcoholic hydrogen chloride, under conditions that succeed with β-naphthol.

Pressure hydrogenation of 2-hydroxy-7-methoxyphenanthrene in the presence of copper chromite gave a mixture of the non-phenolic 1 : 2 : 3 : 4-*tetrahydro*-derivative, which was isolated by means of its picrate, and more fully hydrogenated products, among which the 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-derivative was probably present.

2 : 7-*Dihydroxy*-9 : 10-*dihydrophenanthrene* and its *monomethyl ether* have been prepared and converted into a *dicarboxylic acid* and a *monocarboxylic acid*, respectively, by the Kolbe reaction. Arguing from analogy the carboxyl groups will occupy the symmetrical positions 3 and 6. The yields of these acids were inferior and the projected reduction to pimelic acid derivatives (Einhorn) and subsequent cyclisation was abandoned.

According to Shah and Laiwalla (J., 1938, 1828) a modified Gattermann synthesis enables the formyl group to be introduced into position 3 of methyl β-resorcylate. The Robinson–Schlittler synthesis might be shortened if the *m*-methoxyphenylacetyl group could be similarly introduced. A model experiment with phenylacetyl chloride, however, gave a product that could be converted into 4-phenylethylresorcinol. Accordingly reduction of this to a dihydroresorcinol (the R.–S. type of intermediate) (cf. Hofmann La Roche, E.P. 427,297 of 1937) was not attempted. The Hoesch synthesis using phenylacetonitrile and methyl β-resorcylate did not succeed and the *m*-methoxyphenylacetyl derivative of methylumbelliferone could not be made to undergo a Fries rearrangement (cf. Limaye, *Ber.*, 1932, **65**, 376; Baker, J., 1934, 1954; Russell, Frye, and Mauldin, *J. Amer. Chem. Soc.*, 1940, **62**, 1441, for successful preparations of 2-substituted resorcinols by this method).

2 : 5 : 3′-*Trimethoxydibenzyl* has been prepared in poor yield, but the demethylation of this substance gave tars.

(B) The glycol (I, see above) is a derivative of β-tetralol and it is therefore not surprising that we have been unable to prepare the diketone corresponding to (I). No neutral products were obtained by the use of bromine water or permanganate, though in both cases oxidation was rapid in the cold. Mild treatment with chromic acid gave unidentified ketonic substances. Excess of chromic acid gave a neutral *substance*, probably

(V). Oxidation by the Oppenauer method gave a *substance*, $C_{14}H_{16}O$, the properties of which are best explained by means of the structure (VI).

In another experiment the desired diketone was among the products because a *bisdinitrophenylhydrazone* could be isolated. Attempted dehydrogenation of (I) by means of Raney nickel led to dehydration instead and the dihydro-derivative of (VI) was produced. The same substance resulted from the hydrogenation of 1-γ-ketobutyl-2-benzyloxynaphthalene diethyl ketoacetal.

An attempt to open the heterocyclic ring of (II) by means of acetic anhydride and zinc chloride furnished an unsaturated acetoxy-compound.

Experimental.

(A) 3 : 3′-*Dimethoxydibenzyl.*—(1) *m*-Methoxybenzaldehyde (total, 470 g.) was converted into 3 : 3′-dimethoxybenzoin in the known manner and this was purified only by removal of unchanged and acidic material. A mixture of the crude product (50 g. portions), water (400 c.c.), concentrated hydrochloric acid (400 c.c.), toluene (50 c.c.), and amalgamated zinc (200 g.) was refluxed for 5 hours. The fraction of the product, b. p. 160—190°/2 mm., partly solidified (110 g., total) and by crystallisation of a small part from light petroleum (b. p. 60—80°), 3 : 3′-dimethoxystilbene, m. p. 99°, was isolated (Kopp, *Annalen*, 1893, **277**, 358, gives m. p. 99—100°). The mixed material was hydrogenated in alcohol (800 c.c.), Raney nickel being used at the ordinary temperature and atmospheric pressure. The product (107 g. or 25% overall) solidified to a mass, m. p. 33—35°, raised to the correct m. p., 39—40° on recrystallisation from alcohol.

(2) Schönberg and Malchow (*loc. cit.*) oxidised 3 : 3′-dimethoxybenzoin by means of Fehling's solution. The method of Clarke and Dreyer (*Organic Syntheses*, 1926, **6**, 6) for the oxidation of benzoin has been adapted for work on a larger scale. Crude dimethoxybenzoin (54 g.) was added to a hot solution of hydrated copper sulphate (100 g.) in pyridine (100 g.) and water (40 g.). After stirring for 2 hours at 90—100° the mixture was cooled, and the cake of dimethoxybenzil separated, washed, and dried (45 g., m. p. 78—82°). Crystallisation from aqueous alcohol or benzene gave yellow prisms, m. p. 84° (lit. m. p. 83°). The crude substance was reduced exactly as in (1), including the necessary final catalytic hydrogenation, and 3 : 3′-dimethoxydibenzyl (25 g., or 33% overall) obtained.

(3) Rapson and Robinson (*loc. cit.*) state the method of preparation of *m*-methoxybenzyl chloride but give no details.

Thionyl chloride (148 g.) was gradually added to *m*-methoxybenzyl alcohol (170 g.) and pyridine (100 g.), stirred during 2½ hours below 30°. After ½ hour more, the product was isolated in the known manner; it had b. p. 112—115°/10 mm. (178 g. or 91%).

A mixture of the chloride (100 g.), ether (300 c.c.), and magnesium (8 g.) was gently heated under reflux until ebullition occurred; anhydrous ferric chloride (2·5 g.) was at once added with good stirring. The vigorous reaction that soon set in was controlled by cooling until it subsided (about 15 minutes). The mixture was then stirred and refluxed for an hour. The product was isolated and on distillation methoxybenzyl chloride (4 g.) was recovered. The main fraction (66 g.) had b. p. 203—205°/10 mm., m. p. 38—39° (yield, 89% or 80% from *m*-methoxybenzaldehyde).

6 : 6′-*Di-iodo*-3 : 3′-*dimethoxydibenzyl* (IV).—A solution of 3 : 3′-dimethoxydibenzyl (110 g.) in acetic acid (1000 c.c.) was stirred at 50° and mercuric acetate (160 g.) and powdered iodine (233 g.) were added alternately in small quantities during 1½ hours. The solution was decolorised by means of a little sodium bisulphite, and potassium iodide (200 g.) added. After stirring for 15 minutes, the mixture was poured into water, and the solid product collected. The moist cake was boiled with alcohol (2 l.), the hot solution decanted and cooled, the crystals collected, and the mother-liquor used for another extraction until all the product had been recrystallised in this way. The substance so obtained was already pure, m. p. 113—114°, unaffected by further crystallisation (210 g. or 93%) (Found: C, 38·6; H, 3·2. $C_{16}H_{16}O_2I_2$ requires C, 38·9; H, 3·2%).

2 : 7-*Dimethoxy*-9 : 10-*dihydrophenanthrene.*—A mixture of 6 : 6′-di-iodo-3 : 3′-dimethoxydibenzyl (50 g.) and copper bronze (42 g.) was heated to 230°. An exothermic reaction set in, and was kept under control by occasional removal from the oil-bath, the temperature of which was meanwhile raised to 260°. After about 20 minutes the reaction was allowed to complete itself spontaneously, the internal temperature sometimes rising as high as 280—290°. It was found that if the reaction was controlled too much the yield was inferior. Finally, the mixture was heated for ½ hour at 260°, cooled, and triturated with acetone. The copper residues were removed, the acetone evaporated, and the product distilled, b. p. 180—190°/0·5 mm. (17 g. or 70%). This product was sufficiently pure for the next stage; crystallisation from benzene afforded large, colourless rhombs, m. p. 108—109° (Found: C, 80·1; H, 6·6. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%).

2 : 7-*Dimethoxyphenanthrene* (I, R = R′ = Me).—Dimethoxydihydrophenanthrene (50 g.) was heated with sulphur (7·5 g.) at 220—230° until the evolution of hydrogen sulphide had ceased (about 3 hours). The product was distilled, and the fraction, b. p. 170—200°/0·2 mm., dissolved in hot benzene. On cooling, nearly pure dimethoxyphenanthrene, m. p. 166—168° (30 g. or 60%), separated in colourless crystals. The m. p. was raised to 169—170° by recrystallisation from benzene.

2 : 7-*Dihydroxyphenanthrene* (I, R = R′ = H).—A solution of 2 : 7-dimethoxyphenanthrene (22 g.) in acetic acid (60 c.c.) was boiled, and hydriodic acid (60 c.c., *d* 1·7) added dropwise during 20 minutes. The mixture was boiled until the precipitate obtained on dilution with water dissolved completely in aqueous sodium hydroxide (about ½ hour), and then poured into sodium bisulphite solution (800 c.c. of 1%). The product was dried at 100° (19 g.). Crystallisation from acetic acid gave colourless prisms, m. p. 264° with previous softening. This material (5 g.) in methyl alcohol (50 c.c.) was saturated with hydrogen chloride with cooling in ice; a large proportion of the phenanthrenediol crystallised during this process. After 3 days unchanged 2 : 7-dihydroxyphenanthrene was isolated and no methylation had occurred. The same result followed if the mixture was refluxed for 8 hours. This is a striking contrast with the behaviour of β-naphthol.

2-*Hydroxy*-7-*methoxyphenanthrene* (I, R = H, R′ = Me).—(i) 2 : 7-Dihydroxyphenanthrene and benzoyl chloride were heated at 260° for ½ hour. The product insoluble in alcohol consisted of the *dibenzoate* of 2 : 7-dihydroxyphenanthrene, and crystallised from acetic acid, or better from nitrobenzene, in colourless leaflets, m. p. 252—253° (Found: C, 80·0; H, 4·5. $C_{28}H_{18}O_4$ requires C, 80·4; H, 4·3%).

The crude monobenzoate, soluble in alcohol, was methylated and hydrolysed in the usual way. The phenolic product was sublimed at 250°/10 mm. and crystallised from benzene containing a little alcohol, forming colourless leaflets, m. p. 170—171° (Found: C, 80·7; H, 5·7. $C_{15}H_{12}O_2$ requires C, 80·4; H, 5·4%).

(ii) The following is a better method. Aqueous sodium hydroxide (20 c.c. of 10%) was added to an ice-cooled and well-stirred mixture of 2 : 7-dihydroxyphenanthrene (10·5 g.), acetone (100 c.c.), and methyl sulphate (5·4 c.c.) during 1 hour. An excess of dilute aqueous sodium hydroxide was then added, and the acetone distilled. 2 : 7-Dimethoxyphenanthrene (5 g.) was collected and the filtrate on acidification afforded material from which 2-hydroxy-7-methoxyphenanthrene (4·5 g.) was extracted (Soxhlet, 8 hours) by benzene–light petroleum (b. p. 60—80°, 1 : 1). It had m. p

171—173°, with softening from 167°, and, purified by sublimation at 230°/15 mm., m. p. 173—174° (4 g.). About 0·8 g. of a less pure product was obtained on continuing the extraction for 8 hours, and 0·6 g. of 2 : 7-dihydroxyphenanthrene insoluble in benzene–light petroleum was also obtained.

2-Hydroxy-7-methoxy-1 : 2 : 3 : 4-tetrahydrophenanthrene.—A mixture of 2-hydroxy-7-methoxyphenanthrene (5 g.), alcohol (150 c.c.), and copper chromite (1·5 g.) was stirred and heated at 170—175° for 6 hours under hydrogen at 100 atm. The product was a viscous oil, b. p. 195—200°/0·1 mm. When it was treated with nearly saturated alcoholic picric acid, a crystalline precipitate was thrown down; this was collected after the mixture had been kept for a few hours below 0°. The derivative was decomposed by means of aqueous ammonia and ether. The oil after evaporation of the ether solidified and the *substance* (1·0 g.) crystallised from benzene–light petroleum in small, flat, colourless needles, m. p. 123—124° (Found: C, 78·5; H, 7·1. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·0%).

The substance is insoluble in aqueous sodium hydroxide and the formation of a picrate indicates that it is a naphthalene derivative.

No definite product could be obtained from the residual oily material that did not form a picrate, but treatment with hot hydriodic acid gave largely non-phenolic substances.

3 : 3′-Dihydroxydibenzyl, prepared by demethylation of its dimethyl ether in the manner described above, crystallised from water in long needles, m. p. 139—140° (Found: C, 78·3; H, 6·7. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%).

2 : 7-Dihydroxy-9 : 10-dihydrophenanthrene.—The dimethyl ether (5 g.) was demethylated with hydriodic acid (15 c.c., *d* 1·7) in acetic acid (15 c.c.), as described for 2 : 7-dimethoxyphenanthrene. The product (4·2 g.) crystallised from aqueous acetic acid in colourless leaflets, m. p. 206—208° (Found: C, 78·8; H, 5·5. $C_{14}H_{12}O_2$ requires C, 79·2; H, 5·7%). The *substance* gave a green coloration with aqueous or alcoholic ferric solution.

2-Hydroxy-7-methoxy-9 : 10-dihydrophenanthrene.—Dihydroxydihydrophenanthrene (4·5 g.) was heated with benzoyl chloride (2·5 c.c.) at 210—220° for ½ hour. The product was cooled, powdered, and extracted thrice with boiling alcohol. The residue consisted of *2 : 7-dibenzoyloxy-9 : 10-dihydrophenanthrene*, which crystallised from acetic acid in colourless, slender needles, m. p. 208—210° (Found: C, 80·2; H, 4·9. $C_{28}H_{20}O_4$ requires C, 80·0; H, 4·8%). The filtrate, on concentration, deposited the crude monobenzoate (3·5 g.).

Sodium hydroxide solution (10 c.c. of 50%) was added to the crude monobenzoate (38 g.) dissolved in a mixture of acetone (200 c.c.) and methyl sulphate (11·4 c.c.), and on shaking and heating the reaction was soon completed. An excess of aqueous sodium hydroxide was added, and the mixture refluxed for 1 hour; water was added, and the acetone removed. Neutral material was extracted with ether, and the phenol liberated, collected by means of ether, and distilled, b. p. 215—220°/1—2 mm. (19 g.). The product appeared to contain a trace of dihydroxy-compound, as indicated by its weak green ferric reaction. Extraction of a portion with hot light petroleum and crystallisation of the extract from benzene–light petroleum and finally from benzene gave colourless crystals, m. p. 118—120° (Found: C, 79·5; H, 6·3. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%).

2-Hydroxy-7-methoxy-9 : 10-dihydrophenanthrene-3-carboxylic Acid.—The sodio-derivative of the above monomethyl ether was prepared in alcoholic solution, and dried by evaporation under diminished pressure. The powdered solid (10 g.) was heated with carbon dioxide at 210—220°/20 atms. for 6 hours. The product was dissolved in dilute alkali, and the solution acidified and extracted with ether. The ethereal solution was shaken with sodium bicarbonate solution, which was then acidified. The crystalline precipitate (1·5 g.) was collected and recrystallised from benzene, then from alcohol–benzene, and finally twice from alcohol. The *acid* formed light-brown rhombs, m. p. 225—226° (decomp.) (Found: C, 71·3; H, 5·7. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%). The ferric reaction was deep blue.

2 : 7-Dihydroxy-9 : 10-dihydrophenanthrene-3 : 8-dicarboxylic Acid.—2 : 7-Dihydroxy-9 : 10-dihydrophenanthrene (5 g.) was converted into its disodio-derivative as above. The dry, powdered solid was heated at 200°/5 atms. with carbon dioxide for 7 hours. The acidified product was extracted with ethyl acetate, and the extract shaken with sodium bicarbonate solution; acidification gave the *acid*, which crystallised from methanol in colourless, microscopic rods, m. p. 305° (decomp.) (Found: C, 64·1; H, 4·4. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0%).

2 : 5 : 3′-Trimethoxydibenzyl.—A mixture of *m*-methoxyphenylacetyl chloride (70·4 g.), quinol dimethyl ether (53 g.), and carbon disulphide (200 c.c.) was added to a suspension of aluminium chloride (48 g.) in carbon disulphide (200 c.c.), and the whole refluxed gently with stirring for 10 hours. Next day the product was decomposed with water, and the carbon disulphide removed. The residue was extracted with ether, and the ether shaken with aqueous sodium bicarbonate and then with water. The ether was removed, and the residue distilled in steam, quinol dimethyl ether (17 g.) being recovered. The residue was boiled with amalgamated zinc (250 g.), concentrated hydrochloric acid (500 c.c.), and water (500 c.c.) for 8 hours. The oily product (77 g.) was isolated by means of ether and was largely phenolic. It was methylated by means of sodium hydroxide (200 c.c. of 10%) and methyl sulphate (48 c.c.), acetone (100 c.c.) being added to assist solution. After the first reaction was over, sodium hydroxide (20 g.) and methyl sulphate (30 c.c.) were used in a further methylation. The neutral, oily product was collected by means of ether, freed from solvent, and extracted twice with light petroleum (400 c.c., b. p. 60—80°). The evaporated extract was distilled; the main fraction had b. p. 205—220°/8 mm. The residues from the petroleum extraction were digested with benzene, filtered, and also distilled. The combined distillates were fractionated at a lower pressure; a main fraction (16 g.), b. p. 175—185°/1 mm., and a smaller one (5·5 g.), b. p. 210—220°/1 mm., were then obtained. Most of the product was a resin. The lower fraction was redistilled, giving a nearly colourless oil with a faint blue fluorescence, b. p. 177—180°/0·4 mm. (Found: C, 75·3; H, 7·3. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·3%).

Condensation of Phenylacetyl Chloride with Methyl β-Resorcylate.—Methyl β-resorcylate (5 g.) was suspended in carbon disulphide (45 c.c.), and aluminium chloride (8 g.) added. The solution was cooled and stirred while phenylacetyl chloride (4·6 g.), dissolved in a little carbon disulphide, was added gradually; after 2 hours the mixture was heated gently to complete the reaction. The isolated product, probably *methyl 2-hydroxy-4-phenylacetoxybenzoate*, crystallised from light petroleum (b. p. 40—60°) in flattened needles, m. p. 53—54° (Found: C, 67·1; H, 5·0. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%).

On hydrolysis with alkali β-resorcylic and phenylacetic acids were obtained.

The condensation was therefore carried out in nitrobenzene solution. Powdered aluminium chloride (16 g.) was gradually added to a mixture of methyl β-resorcylate (8·4 g.), phenylacetyl chloride (7·7 g.), and nitrobenzene (45 g.) at 30—40°. After ½ hour the temperature was raised to 50—60°, which was maintained for a further ½ hour. The cooled product was decomposed with dilute hydrochloric acid. The organic layer was diluted with benzene and washed with concentrated sodium carbonate solution, and the solvents removed in steam. The residue, on crystallisation from benzene, gave prisms which on recrystallisation had m. p. 150—151° (Found: C, 67·3; H, 5·1. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%). The alcoholic solution gave a blood-red coloration with ferric chloride. From what follows it is clearly *methyl 2 : 4-dihydroxy-5-phenylacetylbenzoate*. A mixture of the substance (2 g.), alcohol (40 c.c.), amalgamated zinc dust (27 g.), concentrated hydrochloric acid (300 c.c.), water (30 c.c.), and a layer of benzene was refluxed for 4 hours with occasional additions of hydrochloric acid. The zinc residues were collected and washed with benzene. On evaporation of the solvent an oil remained which quickly solidified. Recrystallised from benzene, the substance formed colourless

prisms, m. p. 114—115° (Found : C, 70·3; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%). The ferric reaction in alcohol was a deep blue coloration.

Apparently the methyl ester was not hydrolysed ($C_{15}H_{14}O_4$ requires C, 69·8; H, 5·4%) and the substance is probably *methyl* 2 : 4-*dihydroxy*-5-*phenylethylbenzoate*. The substance (0·5 g.) was heated for 2 hours on the steam-bath with alcohol (15 c.c.) and aqueous sodium hydroxide (5 c.c. of 10%). After removal of most of the alcohol and addition of water the solution was acidified and extracted thrice with ethyl acetate. The extract was evaporated, and the residue refluxed with water (50 c.c.) for 3 hours. After cooling, the product was collected and crystallised twice from water, forming colourless platelets, m. p. 137—138° alone or mixed with authentic 4-phenylethylresorcinol.

Condensation of m-*Methoxyphenylacetyl Chloride with Methyl β-Resorcylate*.—The acid chloride (22 g.) and the ester (20 g.) were dissolved in nitrobenzene (80 g.) and treated at 30° with powdered aluminium chloride (40 g.). The mixture was occasionally shaken and gently heated during 4 hours. Next day it was worked up as before and, on concentration of a benzene solution of the product, crystals of unchanged resorcyclic ester (7 g.) were deposited. The mother-liquors were further concentrated, boiled with alcohol (charcoal), filtered, and concentrated to a small volume. After several days crystals separated and were collected (3 g.) after addition of a little benzene. After repeated crystallisation from benzene, a colourless product was obtained, m. p. 165° with softening from 150°, unchanged by further recrystallisation. Some demethylated product was present (ferric reaction, blood-red).

The crude product was hydrolysed to the corresponding acid by means of aqueous alcoholic sodium hydroxide. The acid, so obtained, crystallised from ethyl acetate in nodules, m. p. 237—240°. It was heated at 240° until carbon dioxide was no longer evolved, and the product dissolved in dilute alkali. The solution was shaken with ether, acidified, and again extracted with ether. The extract was shaken with sodium bicarbonate solution and evaporated. The residual oil solidified, and was crystallised twice from a little acetic acid, then taken up in benzene, and the solution filtered. The filtrate was evaporated, and the residue taken up in a few drops of acetic acid. On keeping, colourless leaflets were deposited. The substance had m. p. 109—110° and gave a blood-red ferric reaction (Found : C, 69·9; H, 5·2. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·4%). Taking the results of the phenylacetylation (above) into consideration, this substance is 4-m-*methoxyphenylacetylresorcinol*.

m-Methoxyphenylacetyl chloride was heated with methylumbelliferone at 140° for ½ hour. Aluminium chloride was then added, and the mixture heated slowly to 170° and maintained at that temperature for an hour. No new product could be isolated from this or a similar experiment in which zinc chloride was employed.

(B) 1-(*γ-Hydroxybutyl*)-2-*hydroxy*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (I)—1-*γ*-Ketobutyl-2-naphthol (20 g.) in alcohol (400 c.c.) was hydrogenated at 155°/75 atms., in the presence of copper chromite (2·5 g.) for 4 hours. The solution was filtered and evaporated under diminished pressure. The residue on distillation gave 18 g., b. p. 200—220°/10 mm., of a colourless, glassy mass. A portion crystallised from benzene–light petroleum gave a *substance*, m. p. 111—112°, which was evidently one of the stereoisomeric forms of the glycol (Found : C, 76·3; H, 9·1. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%). The mother-liquors from the crystallisation were evaporated, and the residue distilled, b. p. 215—220°/10 mm. (Found : C, 76·1; H, 9·0%), showing that the hydrogenation product consisted entirely of the glycol. When the hydrogenation was carried out above 170°, the yield was much lower owing to formation of a chroman derivative.

Oxidation Experiments.—(i) The crude glycol (4 g.) in benzene (30 c.c.) was stirred with an equal volume of water and a mixture of potassium dichromate (4·5 g.), sulphuric acid (6 g.), and water (70 c.c.) was slowly added. When oxidation was complete the benzene solution was separated, washed with sodium carbonate solution, and evaporated. The residue, on distillation, gave a small fraction, b. p. 170—200°/10 mm., and a resinous residue. The distillate was partly ketonic, but no definite product could be obtained from it.

(ii) The glycol (5 g.) in benzene (20 c.c.) was added slowly to a stirred solution of potassium dichromate (30 g.), glacial acetic acid (25 c.c.), sulphuric acid (25 c.c.), and water (150 c.c.). The stirring was continued for 6 hours, with occasional addition of benzene to replace losses by evaporation. Finally the benzene solution was separated, washed with dilute sodium carbonate solution, then with water, and evaporated. The residue on distillation afforded a fraction (1·2 g.), b. p. 150°/0·1 mm., which gave an immediate precipitate with Brady's reagent. The substance crystallised from light petroleum in well-formed, colourless prisms, m. p. 79—80° (Found : C, 72·7; H, 7·0. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). This must be a hydroxy-derivative of the desired diketone, and most probably it is 1-*hydroxy*-1-*γ-ketobutyl*-2-*keto*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (V).

(iii) A mixture of the glycol (5 g.), acetone (120 g.), aluminium *tert.*-butoxide (12 g.), and benzene (250 c.c.) was refluxed for 10 hours. Water was then added, and the benzene layer washed with dilute sulphuric acid and with water, dried, and evaporated. The residue, distilled at 10 mm., gave two fractions, b. p. 155—170° and 185—200°. The higher fraction crystallised on rubbing with light petroleum, and separated from hot light petroleum (b. p. 60—80°) in colourless rosettes, m. p. 110°, undepressed by the crystalline form of the glycol. The lower fraction was a light yellow, mobile oil. It was redistilled, b. p. 156—158°/9 mm. (1·6 g.) (Found : C, 83·5; H, 8·0. $C_{14}H_{16}O$ requires C, 84·0; H, 8·0%). The *substance* gave an amorphous precipitate with Brady's reagent, and instantly decolorised a solution of bromine in carbon tetrachloride. After boiling with water for several hours, the oil decolorised bromine much more slowly. These facts indicate that the substance is the inner anhydride of a keto-alcohol: Such substances are known to react with reagents for ketones, and to be hydrolysed to keto-alcohols on heating with water. Since it is evident that the crystalline form of the glycol was less readily attacked than the other isomer, it is reasonable to assume that the oxidation involved the configuration-determining hydroxyl group and hence we prefer the structure (VI). The alternative in which the side-chain hydroxyl is oxidised and the β-tetralol group is unattacked is not excluded but is regarded as much less probable. Attempts further to oxidise this substance after boiling with water had no useful outcome.

(iv) A mixture of the glycol (6·5 g.), methyl ethyl ketone (10 g.), aluminium *tert.*-butoxide (10 g.), and benzene (250 c.c.) was refluxed for 36 hours. The fraction of the product, b. p. 175—200°/15 mm., was treated with alcoholic 2 : 4-dinitrophenylhydrazine sulphate. The amorphous precipitate was dissolved in the minimum quantity of ethyl acetate and the crystals that separated were collected after 24 hours and recrystallised from dioxan. The stout, four-sided, orange prisms had m. p. 212—213° (decomp.) (Found : N, 19·0. $C_{28}H_{24}O_8N_8$ requires N, 19·4%). Although the yield was unsatisfactory, this *substance* is doubtless a derivative of the diketone corresponding to the glycol.

(v) The glycol (3 g.) was heated under nitrogen at 150—160° for 6 hours with Raney nickel (*ca.* 2 g., washed with ether). On distillation, unchanged glycol was obtained along with a lower fraction, b. p. 156—170°/10 mm. This crystallised from alcohol in colourless prisms, m. p. 72—73°, and was identified with α-methyltetrahydro-5 : 6-benzochroman already described (McQuillin and Robinson, J., 1941, 589). The m. p. previously recorded was 68—69° but a mixture of the two specimens had m. p. 72°. The preparation from the above glycol establishes the constitution of this substance, for which two possibilities were considered.

This methyltetrahydrobenzochroman was also isolated when ketobutylnaphthol was first benzylated, then acetalised by means of ethyl orthoformate and alcoholic hydrogen chloride, and finally reduced in presence of Raney nickel at 100°/100 atms. The product had b. p. 165—180°/10 mm. and crystallised from alcohol in colourless prisms, m. p. 72—73°, alone or mixed with the specimen first obtained.

Perhydro-2-*methyl*-5 : 6-*benzochroman* (II).—A solution of ketobutylnaphthol (15 g.) in alcohol (400 c.c.) was boiled

for 10 minutes with Raney nickel, filtered, and hydrogenated at 180°/125 atms. for 4½ hours in the presence of fresh Raney nickel (*ca.* 5 g.). The product was a colourless, mobile oil, b. p. 135—140°/11 mm. (13 g.). A redistilled fraction, b. p. 132—133°/9 mm., was analysed (Found: C, 80·7; H, 11·5. $C_{14}H_{24}O$ requires C, 80·8; H, 11·5%).

After this *perhydro*-compound had been heated in a sealed tube with an equal weight of acetic anhydride and a little zinc chloride (*ca.* 1% of its weight) at 200° for 6 hours, some unchanged material was recovered. There was also obtained a light yellow oil, b. p. 167—172°/9 mm. (Found: C, 75·5; H, 10·1%). The analysis indicates that this is chiefly an unsaturated monoacetate containing traces of the diacetate of the glycol of which the chroman is the anhydride.

The authors thank the Royal Commission for the Exhibition of 1851 for an Overseas Studentship awarded to one of them.

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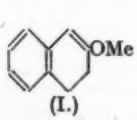
145. *The Preparation of β-Tetralone from β-Naphthol and some Analogous Transformations.*

By JOHN W. CORNFORTH, (MRS.) RITA H. CORNFORTH, and SIR ROBERT ROBINSON.

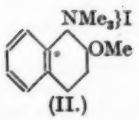
It was already known that the enol methyl ether of β-tetralone may readily be hydrolysed and two examples of the reduction of substituted 2-methoxynaphthalene to dihydro-derivatives are on record. The processes have not, however, hitherto been combined.

We find that 2-methoxynaphthalene may be reduced by sodium and alcohol and that the product on hydrolysis with dilute hydrochloric acid furnishes β-tetralone. It is hard to oxidise β-tetralol in satisfactory yield to the ketone, which becomes readily accessible by the new method for the first time. Substituted 2-methoxynaphthalenes may be similarly converted into β-tetralone derivatives, an interesting application being the conversion of equilenin into a keto-alcohol.

VON BRAUN (*Ber.*, 1930, **63**, 3052) showed that 2-methoxy-3 : 4-dihydronaphthalene (I), obtained by pyrolysis of the quaternary iodide (II), could be hydrolysed to β-tetralone by means of cold dilute hydrochloric acid. This method of preparation of (I) is laborious and expensive. On the other hand, Windaus and Dappe (*Ber.*,



(I.)



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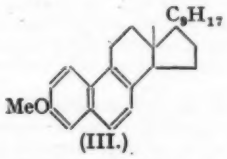

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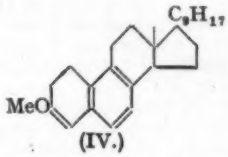
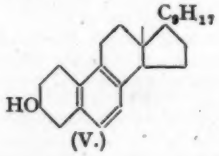


(IV.)

1937, **70**, 76) reduced *O*-methyldehydro*neo*ergosterol (III) to the dihydro-derivative (IV) by means of sodium and propyl alcohol, but did not hydrolyse the substance to a ketone.



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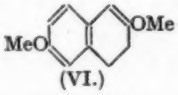

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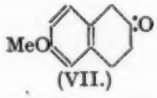

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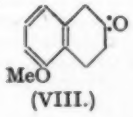


(VIII.)

The constitution (IV) was based on the absorption spectrum of the substance and on its conversion into (V) by catalytic hydrogenation in ether–acetic acid solution.

Similarly Robinson and Weygand (J., 1941, 386) reduced 2 : 6-dimethoxynaphthalene to a dihydro-derivative by means of sodium and *iso*amyl alcohol but did not hydrolyse the product (VI) to 6-methoxytetralone (VII). The latter stage has now been carried out and the ketone proved to be identical with a specimen synthesised by the method of Crowley and Robinson (J., 1938, 2001).

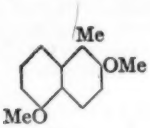
In the case of 2-methoxynaphthalene, sodium and methyl alcohol do not effect reduction and the yield of tetralone when propyl alcohol was used was inferior. The best results were obtained with sodium and ethyl alcohol, the yield of ketone obtained on hydrolysis of the product being 56%, and this can probably be improved.

Analogously, 2-methoxy-1-methylnaphthalene afforded 1-*methyl*-β-*tetralone* in 10% yield. Here reduction also occurred in the unsubstituted nucleus and 2-methoxy-1-methyl-5 : 6 : 7 : 8-tetrahydronaphthalene was isolated from the products of the reaction.

Reduction, followed by hydrolysis, of 1 : 6-dimethoxynaphthalene furnished 5-*methoxy*-2-*tetralone* (VIII) in good yield. On the other hand, the reduction and later hydrolysis of 2 : 5-*dimethoxy*-1-*methylnaphthalene* (IX) (1 : 6-dimethoxy-5-methylnaphthalene) gave the β-tetralone (X) and a small quantity of the α-tetralone (XI). The methylation of β-tetralone by means of methyl iodide and sodium *iso*propoxide in *iso*propyl-alcoholic solution (cf. Suter and Weston, *J. Amer. Chem. Soc.*, 1942, **64**, 533) afforded 1-methyl-β-tetralone, but when (VIII) was treated in this way the product was a dimethyl derivative, probably 5-*methoxy*-1 : 1-*dimethyl*-β-*tetralone*.

When equilenin methyl ether is reduced by means of sodium and alcohol, and the product hydrolysed, the

keto-alcohol (XII) is produced. This observation opens up many possibilities of synthesis of potentially androgenic substances and the physiological properties of (XII) will be examined.



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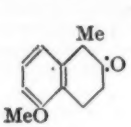

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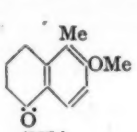
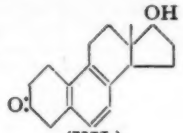
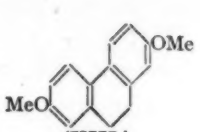


(XI.)



(XII.)



(XIII.)

Reduction of 2 : 7-dimethoxyphenanthrene gave only the 9 : 10-dihydro-derivative (XIII) (Cornforth and Robinson, preceding paper). Hence the reaction is general only for true 2-methoxynaphthalenes.

β-Tetralone is characterised by the blue coloration produced when it is treated with alcoholic sodium hydroxide in the presence of air. This reaction is given by all the β-tetralones (including XII) that we have examined, but not by those bearing substituents in the 1-position. Tetralone-blue is changed by acid to an orange-coloured substance, and it is noteworthy that both the blue and the orange colour are extractable by benzene. The reversible change is effected by ammonia and carbon dioxide and hence occurs at about p_H 7.

Experimental.

β-Tetralone.—Sodium (20 g.) was added during 10 minutes to a solution of 2-methoxynaphthalene (16 g.) in commercial " absolute " alcohol (200 c.c.) heated under reflux (bath at 115°). Heating was continued until all the metal disappeared; the cooled solution was then diluted with water (200 c.c.), and concentrated hydrochloric acid (200 c.c.) added as rapidly as possible (otherwise " tetralone-blue " is formed). The mixture was heated on the steam-bath for 15 minutes with occasional shaking, then cooled and shaken with ether. The oil from the washed extract was shaken with concentrated sodium bisulphite solution (70 c.c.). The crystals that soon separated were collected after ½ hour, washed well with ether, and decomposed either by warming with 10% hydrochloric acid or by sodium carbonate solution in the cold. The ketone was isolated by means of ether and distilled as an almost colourless oil, b. p. 130—131°/11 mm. (yield, 8·2 g. or 56%). The ketone was characterised as the phenylhydrazone

1-*Methyl-β-tetralone.*—2-Methoxy-1-methylnaphthalene (17 g.) was reduced as above with sodium (20 g.) and alcohol (200 c.c.). The oil isolated after hydrolysis with acid was treated with semicarbazide hydrochloride (5 g.) and sodium acetate (7·5 g.) in aqueous alcohol (50 c.c.), and the mixture kept overnight. The solid was collected, washed with alcohol, water, and again alcohol, and dried (2 g., 10%). A portion recrystallised from alcohol gave 1-*methyl-β-tetralone semicarbazone* in fine colourless needles, m. p. 200—202° (decomp.) (Found : N, 19·4. $C_{13}H_{15}ON_3$ requires N, 19·4%). Another portion was hydrolysed by warming with 10% hydrochloric acid; the ketone was isolated by means of ether and distilled. 1-*Methyl-β-tetralone* is a colourless oil, b. p. 137—138°/18 mm. (Found : C, 82·7; H, 7·7. $C_{11}H_{12}O$ requires C, 82·5; H, 7·5%).

In another experiment the oil after hydrolysis was distilled under diminished pressure. The distillate deposited crystals, which were recrystallised from alcohol. The substance had m. p. 51°, alone or mixed with authentic 2-methoxy-1-methyl-5 : 6 : 7 : 8-tetrahydronaphthalene kindly supplied by Dr. R. Martin (new substance, private communication).

5-*Methoxy-β-tetralone* (VIII).—1 : 6-Dimethoxynaphthalene (10·5 g.) was reduced with sodium (11 g.) and alcohol (120 c.c.), the product hydrolysed, and the ketone isolated as the bisulphite compound. This was best decomposed by solution in water and addition of sodium carbonate solution. The *ketone* was isolated by means of ether and distilled as a colourless, viscid oil, b. p. 120—122°/0·4 mm. (6·2 g.; 63%) (Found : C, 74·6; H, 7·1. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%). With alcoholic alkali a fine purple coloration was developed, more slowly than with β-tetralone.

6-*Methoxy-β-tetralone.*—A mixture of the dihydro-derivative of 2 : 6-dimethoxynaphthalene (2 g.) (Robinson and Weygand, *loc. cit.*), alcohol (20 c.c.), and hydrochloric acid (5 c.c. of 10%) was heated on the steam-bath for 10 minutes, water (50 c.c.) added, and the cooled mixture stirred until the oil crystallised. The solid, drained free from oil, crystallised from light petroleum (b. p. 40—60°) in colourless needles, m. p. 36·5°. This material (1 g.) was mixed with 0·5 g. of 6-methoxy-β-tetralone (Crowley and Robinson, *loc. cit.*) which was not quite pure; the whole on crystallisation gave needles, m. p. 36°

2 : 5-*Dimethoxy*-1-*methylnaphthalene.*—6-Methoxy-5-methyl-α-tetralone (30 g.) was heated with sulphur (3·75 g.; 75% of the theoretical amount) at 220—225° for 1½ hours. The phenolic product was separated and methylated with methyl sulphate and sodium hydroxide; the neutral product was again dehydrogenated, and the phenols separated and methylated as before. The combined methylated products were distilled, b. p. 190—191°/16 mm. (21 g.). The distillate crystallised immediately; a portion, recrystallised from alcohol, formed fine hexagonal plates, m. p. 85° (Found : C, 77·2; H, 6·9. $C_{13}H_{14}O_2$ requires C, 77·2; H, 6·9%).

5-*Methoxy*-1-*methyl-β-tetralone* (X).—2 : 5-Dimethoxy-1-methylnaphthalene (10 g.) was reduced with sodium (10 g.) and alcohol (100 c.c.). The oil isolated after hydrolysis with acid was treated with semicarbazide acetate, and the solid collected, washed with water and alcohol, and dried (4 g.). A portion after two crystallisations from alcohol gave 5-*methoxy*-1-*methyl-β-tetralone semicarbazone* in small, four-sided prisms, m. p. 188—190° (Found : C, 63·2; H, 7·3; N, 16·9. $C_{13}H_{17}O_2N_3$ requires C, 63·2; H, 6·8; N, 17·0%). This semicarbazone, the main product, is not identical with the semicarbazone of 6-methoxy-5-methyl-α-tetralone (XI). (The latter ketone is an intermediate in another investigation in progress in this laboratory.) Hence it follows that it must be a derivative of the expected β-tetralone.

The *crude* semicarbazone (3 g.) was hydrolysed by heating for a short time with 10% hydrochloric acid (20 c.c.), and the product (2 g.) isolated by distillation at 0·2 mm. (bath at 130—140°). A portion of the distillate was converted into the 2 : 4-dinitrophenylhydrazone, which was crystallised from acetic acid. A few deep red crystals were the first to separate, and these were collected before the main crop could be deposited. The red material after another crystallisation from acetic acid formed leaflets with a metallic glance, m. p. 249—250°, undepressed by the 2 : 4-dinitrophenylhydrazone of 6-methoxy-5-methyl-α-tetralone (XI).

C-*Methylation of β-Tetralone.*—Sodium (1·26 g.) was dissolved in dry *iso*propyl alcohol (40 c.c.). Air was displaced from the apparatus by nitrogen, and β-tetralone (8 g.) added. The solution was then cooled in ice during the gradual addition of methyl iodide (10·9 g.) in *iso*propyl alcohol (25 c.c.), and the reaction finally completed by refluxing on the steam-bath for 2 hours. After dilution and acidification out of contact with the atmosphere, the oily product was isolated by means of ether and shaken with saturated aqueous sodium bisulphite (50 c.c.). After ½ hour the bisulphite compound was collected and washed with ether. The ethereal filtrate was washed with water, dried, and evaporated, and the residue distilled as a colourless oil, b. p. 137—138°/18 mm. (5·2 g.); 1·5 g. of β-tetralone were recovered from the bisulphite

compound. The alcoholic alkali test revealed the presence of only a trace of unchanged β-tetralone, and the identity and homogeneous nature of the product were shown by preparation of the semicarbazone, which after a single crystallisation had m. p. 200—202°, undepressed by the semicarbazone of 1-methyl-β-tetralone previously described.

5-Methoxy-1 : 1-dimethyl-β-tetralone.—The methylation of 5-methoxy-β-tetralone (6 g.) was carried out as described for β-tetralone. The product (2·5 g.) had b. p. 105—110°/0·2 mm. It partly crystallised and was recrystallised from light petroleum, forming colourless rhombic plates, m. p. 77—79° (1·2 g.). Another crystallisation from methyl alcohol raised the m. p. to 83—85° (Found : C, 76·1; H, 7·4. $C_{13}H_{16}O_2$ requires C, 76·5; H, 7·8%).

The *semicarbazone* crystallised from alcohol in colourless rods, m. p. 192—194° (Found : N, 16·1. $C_{14}H_{19}O_2N_3$ requires N, 16·1%).

The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in orange-yellow needles, m. p. 184° (Found : N, 14·8. $C_{19}H_{20}O_5N_4$ requires N, 14·6%).

Reduction of Equilenin Methyl Ether.—Equilenin (2 g.) was methylated with sodium hydroxide and methyl sulphate, and the precipitated ether washed and dried at 100°. It was dissolved in alcohol (100 c.c.) and reduced with sodium (10 g.). The reaction mixture was worked up as described for β-tetralone, and a bisulphite compound obtained, which was dissolved in water and decomposed by sodium carbonate. The product was taken up in ether, and the dried extract evaporated; the residue (0·8 g.) crystallised at once. It was sublimed at 160—170°/0·3 mm. and crystallised from benzene. The product (XII) formed rhombic platelets, m. p. 152—153° (Found : C, 79·8; H, 8·3. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·1%). $[\alpha]_D^{22°}$ +33·6° (*c*, 3·3 in ethanol). With alcoholic alkali the substance gave a green fluorescence, which vanished slowly as a deep purple colour developed.

Reduction of 2 : 7-Dimethoxyphenanthrene.—2 : 7-Dimethoxyphenanthrene (5 g.) was reduced with sodium (25 g.) and alcohol (300 c.c.), the large amounts being rendered necessary by its sparing solubility. The solution was hydrolysed in the usual way. The resulting oil partly crystallised on keeping. The crystals were recrystallised from benzene, forming rhombic prisms, m. p. 108—109°, undepressed by 2 : 7-dimethoxy-9 : 10-dihydrophenanthrene. The non-crystalline fraction gave ketonic reactions, but no pure substance could be isolated.

The authors are grateful to the Royal Commissioners of the Exhibition of 1851 for Overseas Scholarships awarded to two of them.

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, August 4th*, 1942.]

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146. *Decalin*-1 : 5-*dione and* 2 : 2′-*Diketodi*cyclo*pentyl*.

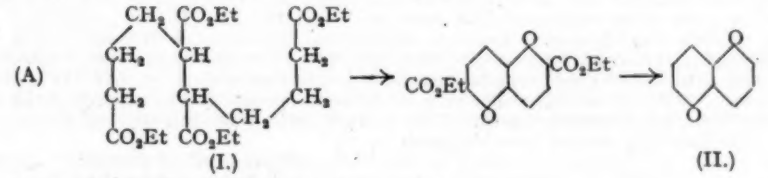
By B. J. F. HUDSON and SIR ROBERT ROBINSON.

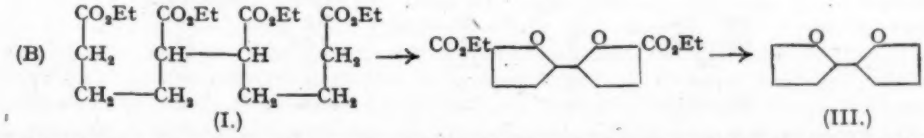
The double Dieckmann-type of cyclisation of *ethyl octane*-1 : 4 : 5 : 8-*tetracarboxylate* might give a naphthalene or a di*cyclo*pentyl derivative. We were interested in the former possibility, but the reaction takes the latter course. The *diketodi*cyclo*pentyl* which was obtained on hydrolysis of the product was independently synthesised.

Decalin-1 : 5-*dione* has been obtained by catalytic reduction of 1 : 5-dihydroxynaphthalene, followed by oxidation of the decalin-1 : 5-diol produced, but the yields were unsatisfactory.

So far as we are aware the only decalindiones that have been described are two in which both keto-groups are situated in one *cyclo*hexane ring (cf. Ganapathi, *Current Sci.*, 1938, **6**, 448; Chuang and Tien, *Ber.*, 1936, **69**, 25). Diketones which are fused *cyclo*hexanones are of interest in view of the possibility of building on two more rings and in the first instance we have examined methods for the synthesis of decalin-1 : 5-dione because of its symmetry.

Ethyl octane-1 : 4 : 5 : 8-*tetracarboxylate* (I) was obtained by the action of silver powder on ethyl α-bromoadipate. Its cyclisation might proceed according to (A) or (B); analogy for (A) is found in the formation of chrysene derivatives from ββ′-diaryladipic acids, and for (B) in the synthesis of indigotin from dianilinomaleic acid.





The cyclisation with sodium was unsuccessful, but with potassium a keto-ester was obtained which on hydrolysis afforded diketones, $C_{10}H_{14}O_2$. The product melted over a range of temperature and may have contained some of the desired decalindione (II), but it consisted essentially of (III). This 2 : 2′-*diketodi*cyclo*pentyl* was prepared in a purer condition by hydrolysis of the product of oxidation of ethyl sodio*cyclo*pentanone-2-carboxylate with iodine. Catalytic hydrogenation of 1 : 5-dihydroxynaphthalene at 120—180°/10—20 atms. over a nickel–kieselguhr catalyst affords 5-hydroxy-1-tetralone (Schroeter and Tetralin G.m.b.H., G.P. 352,720) but the yield was not stated. At higher pressures (120 atms.) with Raney nickel at 100—150°, the chief products are α-decalols but 5—8% of x-*decalin*-1 : 5-*diol* could be isolated. The substance is apparently

a stereoisomeride of the decalin-1 : 5-diol reported by Campbell and Harris (*J. Amer. Chem. Soc.*, 1941, **63**, 2721). These authors oxidised $\Delta^{9:10}$-octalin by means of selenium dioxide in acetic anhydride solution at 30°, thereby introducing two acetoxyl groups. The product was hydrolysed and oxidised to an octalindione. The latter (0·3 g.) on dehydrogenation and acetylation of the product afforded a few mg. of 1 : 5-diacetoxynaphthalene. Although the yield was small, this is not unusual in such dehydrogenations, and the experiment seems to be conclusive in view of the sharp m. p. of the octalindione. Our *x*-decalin-1 : 5-diol could be oxidised by chromic acid to the diketone (II), which was obtained in two stereoisomeric forms, of which that of higher melting point is regarded as derived from *trans*-decalin. In view of other interests the work has been temporarily abandoned.

Experimental.

Ethyl Octane-1 : 4 : 5 : 8-*tetracarboxylate* (I).—Silver powder prepared by either of the following methods was used: (1) Freshly precipitated silver chloride was mixed with an excess of aqueous sodium hydroxide (10%), and formalin (33%) added very gradually. The reduction was completed by heating on the steam-bath, and the silver collected, washed, and dried. (2) A dilute solution of silver nitrate was stirred with an equivalent of copper bronze until reduction appeared complete. The presence of traces of copper in the product was an advantage.

A mixture of ethyl α-bromoadipate (100 g.) (Ingold, J., 1921, **119**, 316) and silver powder (50 g.) was vigorously stirred and heated to 140—160°. After 2 hours the mixture was cooled and filtered, and the silver bromide washed with ether. The dry solid (80 g., indicating complete removal of bromine) was triturated with aqueous sodium hydroxide and formalin, and the silver used again. On distillation of the residue after removal of ether, 40—50% of ethyl adipate was first obtained, b. p. 90—174°/0·2—0·3 mm. and largely b. p. 90—110°; redistilled, b. p. 245°/760 mm., $n_D^{20°}$ 1·4300. The second fraction, b. p. 180—200°/0·2—0·3 mm., was redistilled, b. p. 192—195°/0·2—0·3 mm. (21·9 g.; 31%), $n_D^{20°}$ 1·4518 (Found: C, 59·5; H, 8·2. $C_{20}H_{34}O_8$ requires C, 59·7; H, 8·5%).

2 : 2′-*Diketodi*cyclo*pentyl* (III).—(A) Ethyl *cyclo*pentanone-2-carboxylate (14·4 g.) was added slowly to a suspension of sodium powder (2·4 g.) in dry ether (150 c.c.). After subsidence of the initial reaction the mixture was refluxed for 3 hours, cooled, and stirred while iodine (9·6 g.) in ether (150 c.c.) was introduced during 2 hours. After being stirred for 1 hour more, the liquid was filtered and evaporated, leaving an orange-red oil that decomposed on attempted distillation. The crude product was refluxed with a solution of sodium hydroxide (3 g.) in water (70 c.c.) and alcohol (30 c.c.) for 3 hours. The neutral product was isolated by means of ether and distilled. After removal of a considerable amount of *cyclo*pentanone, a fraction, b. p. 124—128°/15 mm., was obtained as a light yellow oil which partly solidified at 0°. The drained solid crystallised from light petroleum (b. p. 40—60°) in colourless needles, m. p. 67—69° (Found: C, 72·0; H, 8·6. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%). The overall yield was only 2—4%.

(B) Reaction occurred when a mixture of ethyl octane-1 : 4 : 5 : 8-tetracarboxylate (16·0 g.), potassium powder (4·1 g.), and toluene (20 c.c.) at 0° was allowed to reach the room temperature. The orange-coloured oily product (31 g.) from three such experiments, worked up in the known manner, was hydrolysed by refluxing for 5 hours with hydrochloric acid (30 c.c., *d* 1·16), alcohol (45 c.c.), and water (85 c.c.). The neutral product was isolated by means of ether and distilled, b. p. 100—120°/0·2—0·3 mm. (3·9 g.; 20%) (Found: C, 71·6; H, 8·6%), $n_D^{20°}$ 1·4880. This material slowly solidified and on recrystallisation from light petroleum (b. p. 40—60°) had m. p. 48—54° (Found: C, 72·1; H, 8·5%). A mixture with the product from (A) had m. p. 55—65°. Further crystallisation raised the m. p. to 51—65° and this, mixed with the product from (A), had m. p. 62—68°. These results indicate admixture with some other substance, possibly decalin-1 : 5-dione, but it is clear that the material is essentially diketodi*cyclo*pentyl.

The *bis*-2 : 4-*dinitrophenylhydrazone* crystallised from acetic anhydride in reddish-orange needles, m. p. 230—240° (decomp.) (Found: N, 21·2. $C_{32}H_{32}O_8N_8$ requires N, 21·3%). The semicarbazone was anomalous (N, 25·9%), but the same substance, m. p. 230—240° (decomp.) (N, 25·5%), was obtained from the product of the action of sodium on the tetracarboxylic ester and subsequent hydrolysis.

The diketone (1·6 g.) was methylated by means of sodamide (1·6 g.) and methyl iodide (6 g.) in ethereal solution under the usual conditions. The fraction of the product, b. p. 175—185°/14 mm., was converted into a *dioxime*, which formed white crystals, m. p. 207—211° (decomp.), from methyl alcohol (Found: N, 13·3. $C_{11}H_{12}O_2N_2$ requires N, 13·3%). From this result it appears that one methyl group was introduced ($C_{10}H_{16}O_2N_2$ requires N, 14·4 and $C_{12}H_{20}O_2N_2$ requires N, 12·5%).

x-*Decalin*-1 : 5-*diol*.—1 : 5-Dihydroxynaphthalene (32 g.) in ethanol (60 c.c.) along with a catalyst (2 g. of Raney nickel or copper chromite) was heated at 150—200° with hydrogen (120 atms.) for 8 hours. The phenolic and the neutral products were separated, and the latter distilled. The fraction, b. p. 115—150°/15 mm., consisted chiefly of mixed α-decalols. On keeping, crystals were deposited and recrystallisation from aqueous methanol, light petroleum (b. p. 60—80°), and acetone afforded *cis*-1-decalol, long needles, m. p. 92—94°. The second fraction, a viscous oil, b. p. 175—180°/15 mm., solidified and then crystallised from benzene in colourless prisms, m. p. 137—147° (Found: C, 70·5; H, 10·7. $C_{10}H_{18}O_2$ requires C, 70·6; H, 10·6%). The m. p. of different specimens was variable in the range 130—150°. By repeated crystallisation from ethyl acetate a product, m. p. 159—161°, was obtained and this is possibly an individual stereoisomeride. The following results were obtained:

Catalyst.	Temp.	Time, hrs.	Pressure.	Crystalline 1 : 5-diol, g.	Other non-phenolic, g.	Phenolic, g.
Ni	150—200°	8	to 120 atms.	2·5	28	—
Ni	100—150	3	,, 120 ,,	2·6	26	3
Ni	150	5	,, 110 ,,	2·5	22	trace
Ni	100	4	,, 100 ,,	2·1	23	2—3
CuCrO	220—250	36	,, 150 ,,	none	2	*ca.* 25

The phenolic product from the last-mentioned experiment constituted 90% of the whole. On distillation it gave 12 g. (b. p. 125—130°/15 mm.) of 5 : 6 : 7 : 8-tetrahydro-1-naphthol. The substance crystallised from light petroleum (b. p. 60—80°) in colourless plates, m. p. 65° (Found: C, 80·7; H, 8·3. Calc. for $C_{10}H_{12}O$: C, 81·0. H, 8·2%). Crystallisation of the residue from alcohol and from benzene afforded greenish-grey needles, m. p. 165—170° (Found: C, 77·7; H, 7·5%). The acetate had m. p. 129—131° (Found: C, 72·2; H, 6·9%). This substance has not been identified.

Decalin-1 : 5-*dione* (II).—(A) A solution of chromic anhydride (6·4 g., four times the theoretical amount) in water (5 c.c.) and acetic acid (40 c.c.) was added dropwise to one of decalin-1 : 5-diol (2 g., crystallised from ethyl acetate) in acetic acid (10 c.c.) at 0° with good stirring. The mixture was allowed to reach the room temperature and kept for 18 hours. The solvent was removed by vacuum distillation through a column, the residue mixed with water, and the product isolated by means of ether. The yellow oil solidified and crystallisation from benzene afforded colourless needles, m. p. 165—167° (0·2 g.; 10%) (Found: C, 72·4; H, 8·2. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·5%).

(B) When decalin-1 : 5-diol (2·3 g.) in acetic acid (10 c.c.) was similarly treated with chromic anhydride (3·7 g., twice the theoretical amount) in water (3 c.c.) and acetic acid (20 c.c.), and the product worked up as before, evidence was obtained of the formation of a mixture of stereoisomerides. Crystallisation from light petroleum (b. p. 60—80°) furnished 0·6 g., m. p. 70—140°, and from the mother-liquor 0·4 g., prisms, m. p. 72—79° (total yield, 25%). Recrystallisation of the first crop from benzene–light petroleum gave 0·5 g. of a mixture of prisms and needles, m. p. 85—100° (Found: C, 72·1; H, 8·4%).

(C) Reduction of the quantity of chromic anhydride to 1·25 times the theoretical amount increased the yield to 60%. The product was separated into two fractions, the less soluble having m. p. 85—115° and closely resembling the mixture of similar m. p. obtained in (B). The more soluble fraction, prisms, m. p. 68—72° (about 1/4 of the whole product), is probably the nearly pure stereoisomeride of the former, m. p. 164—167° (A, above) (Found: C, 72·2; H, 8·6%).

This substance and also the mixtures, m. p. 85—100° and the like, may be converted into the isomeride, m. p. 164—167°, by heating with acetic acid for 6 hours at 100°.

All analogy points to the allocation of the *trans*-decalin configuration to the form of the higher m. p.

In the first place the hydrogenation of α-naphthol yields *cis*-1-decalol (cf. Hückel, *Annalen*, 1925, **441**, 1) and we have obtained this substance in considerable amount as a by-product of the hydrogenation of 1 : 5-dihydroxynaphthalene. Hence it is probable that the mixed decalindiols obtained by us are predominantly derived from *cis*-decalin; four such isomerides are possible, but these should yield only one diketone. Oxidation under the milder conditions affords the more fusible, more soluble diketone (cf. *cis*-1-decalone, m. p. 2°; *trans*-1-decalone, m. p. 33°). Finally *cis*-1-decalone is labile and may be transformed into *trans*-1-decalone in the presence of basic or acidic catalysts.

When *cis*- or *trans*-decalin-1 : 5-dione, or a mixture of these, was heated with methanolic potassium hydroxide, a series of colour changes occurred and eventually the solution became yellowish-brown. On the addition of water a neutral substance (m. p. *ca.* 143°) was precipitated. Acidification of the filtrate afforded 5-hydroxy-1-tetralone (Schroeter, *loc. cit.*). The substance, from mixed diketones, crystallised from ether–light petroleum (b. p. 40—60°) in prismatic needles, m. p. 154—156° (pure, m. p. 157°) and gave a 2 : 4-dinitrophenylhydrazone. The orange-yellow *p*-nitrobenzeneazo-derivative dissolved in alcoholic sodium hydroxide to a permanganate-coloured solution.

Diphenylhydrazone of trans-*Decalin*-1 : 5-*dione*.—This *derivative* separated immediately when phenylhydrazine (excess) was added to a cold solution of the diketone in acetic acid; pale yellow, short, prismatic needles, m. p. 230° (Found in material dried at 100°: C, 76·0; H, 7·3. $C_{22}H_{26}N_4$ requires C, 76·3; H, 7·5; N, 16·2%). The corresponding derivative from *cis*-decalin-1 : 5-dione, m. p. 68—72°, crystallised more slowly from the reaction mixture in pale yellow, prismatic needles, m. p. 172—173° to a gum which cleared at 208—210° (Found: N, 15·8%). This behaviour suggests that the substance contains some of the *trans*-compound or that conversion into the latter occurs in the process of heating.

3 : 4 : 7 : 8 : 9 : 10-*Hexahydronaphtha*(1 : 2 : 5 : 6)-*bis*-(2 : 3)-*indole*.—The diphenylhydrazone of the *cis*-diketone is converted into this substance by boiling acetic acid or more readily by hot alcoholic or aqueous alcoholic hydrochloric acid. Hydrogen chloride was passed rapidly into an alcoholic suspension until the liquid boiled and for a minute longer. The orange solution gave an ochreous precipitate on dilution with water; this was collected and crystallised from alcohol, in which it was moderately sparingly soluble, forming colourless, short needles, m. p. 312—316° (decomp.) (Found in material dried at 100°: C, 84·2; H, 6·5; N, 8·8. $C_{22}H_{20}N_2$ requires C, 84·6; H, 6·4; N, 9·0%). No coloration was developed with *p*-dimethylaminobenzaldehyde and aqueous alcoholic hydrochloric acid in the cold; on boiling, the liquid gradually became dichroic, brownish-green and red, and, on cooling, yellowish-brown; these effects can be alternated.

When similarly treated, the diphenylhydrazone of the *trans*-diketone afforded a substance that crystallised from alcohol, in which it was very sparingly soluble, in short microscopic needles showing a pronounced tendency to form X-shaped twins, m. p. 292—296° (decomp.) (Found: C, 74·3; H, 6·5; N, 8·1%). The substance apparently contains $C_{22}N_2$ and oxygen. Whereas the true bis-indole may be rapidly distilled up a tube, this compound suffers complete decomposition.

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147. *New Syntheses of Heterocyclic Compounds. Part I. 2 : 3-Dialkylquinolines.*

By VLADIMIR A. PETROW.

The reaction of anils, prepared by the condensation of the formyl derivatives of certain ketones with primary arylamines, with arylamine hydrochlorides leads under well-defined conditions to ring closure. The synthesis has been applied to the preparation in excellent yields of six types of heterocyclic systems. By selecting suitable derivatives of aniline, a large variety of substituted tetrahydroacridines has been obtained.

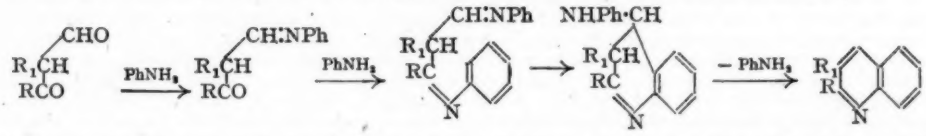
β-DIKETONES react with arylamines to give unsaturated products readily convertible into quinolines (Combes, *Compt. rend.*, 1887, **106**, 142). Substituted diketones behave in a similar way, Combes (*ibid.*, p. 1536) preparing 2 : 3 : 4-trimethylquinoline from methylacetylacetone. Borsche (*Ber.*, 1908, **41**, 2203) obtained a difficultly separable mixture of anilides from 1-acetyl*cyclo*hexan-2-one, which passed severally, on cyclisation, into 5-methyl-1 : 2 : 3 : 4-tetrahydroacridine and 10-methyl-1 : 2 : 3 : 4-tetrahydrophenanthridine. β-Keto-esters have also been used; Conrad and Limpach (*Ber.*, 1887, **20**, 944) obtained β-phenylaminocrotonic ester, which passed into 4-hydroxyquinaldine on dehydration, and substituted acetoacetic esters have been used by Dieckmann (*Annalen*, 1901, **317**, 91) and Sen and Basu (*J. Indian Chem. Soc.*, 1930, **7**, 435).

Attempts to carry out analogous condensations with β-keto-aldehydes have been only partially successful. Borsche (*Annalen*, 1910, **377**, 70) condensed formyl*cyclo*hexanone with aniline, but failed to cyclise the resulting 1-phenyliminomethyl*cyclo*hexan-2-one. Thielepape (*Ber.*, 1922, **55**, 127) attributed his lack of success with phenyliminomethylacetone (from formylacetone) to a *trans*-configuration of the anil. Romet (*Compt. rend.*, 1935, **200**, 1676) obtained a low yield of 3-methyl-2-ethylquinoline together with a smaller amount of the 3-methyl-4-ethyl isomeride from 2-phenyliminomethylpentan-3-one (from formyldiethyl ketone) by fusion with anhydrous zinc chloride, or by refluxing with this reagent in *iso*amyl-alcoholic solution. In an attempt to

develop this synthesis, 1-phenyliminomethyl*cyclo*hexan-2-one (Borsche, 1910, *loc. cit.*) was recovered unchanged after 10 hours' refluxing with the latter reagent. Considerable resinification occurred on fusion with anhydrous zinc chloride, but crude picrates were obtained in *ca.* 5% yield, so the synthesis resembles the production of acridine in 0·5% yield from salicylideneaniline by prolonged fusion with zinc chloride (Mohlau, *Ber.*, 1886, **19**, 2451). Sen-Gupta (J., 1915, **107**, 1347) prepared 3-cyano-2-ketohexahydroquinoline from formyl*cyclo*hexanone and cyanoacetamide. Basu (*Annalen*, 1934, **512**, 131) obtained ethyl 2-methyl-5 : 6 : 7 : 8-tetrahydroquinoline-3-carboxylate from formyl*cyclo*hexanone and ethyl β-aminocrotonate. Hydroxyquinolines have been prepared from formylacetic ester (Wislicenus, *Annalen*, 1917, **413**, 248) and from formylphenylacetic ester (Wislicenus and Erbe, *ibid.*, 1920, **421**, 146).

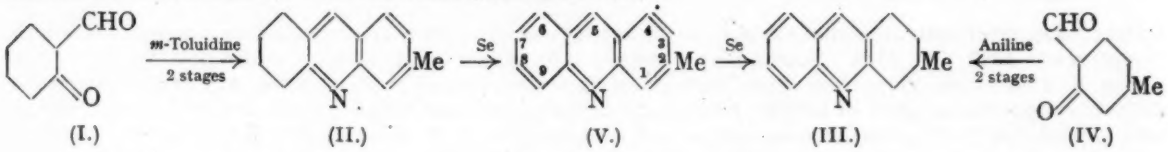
A new method whereby aliphatic β-keto-aldehydes, *i.e.*, the formyl (hydroxymethylene) derivatives of aliphatic ketones of the type $R{\cdot}CO{\cdot}CH_2R_1$ (where R and R_1 are alkyl groups), may be converted in *ca.* 50% yield into 2 : 3-dialkylquinolines consists in condensing the formyl derivative with the primary aromatic amine (1 mol.) to give quantitatively the anil $R{\cdot}CO{\cdot}CH(CH{:}NAr){\cdot}R_1$ and heating this product with the amine hydrochloride (1 mol.), either directly at 160—200° or in absolute alcoholic solution. The yield may be increased to 65% by using 2 mols. of the amine hydrochloride and 1 mol. of anhydrous zinc chloride to each mol. of the anil. The anils have in general been isolated, but this is not essential, as the crude condensation products may be used with equal success.

By analogy with salicylideneaniline, to which a *trans*-configuration has been assigned on the evidence of absorption spectra measurements (Hendricks, Wulf, Hilbert, and Liddel, *J. Amer. Chem. Soc.*, 1936, **58**, 1991), dipole moment measurements (de Gaouck and Le Fèvre, J., 1938, 741), and the formation of chelate metallic salts (Hunter and Marriott, J., 1937, 2000), it may be inferred that the anils derived from β-keto-aldehydes are similarly oriented. Their direct cyclisation is therefore improbable on stereochemical grounds. Again, direct cyclisation would give 3 : 4-dialkyl quinolines, whereas the 2 : 3-dialkyl isomerides are actually obtained (cf., however, Romet, *loc. cit.*). Intramolecular rearrangement of the anils would hardly take place in boiling alcoholic solution; production of the 2 : 3-dialkylquinolines therefore probably occurs as follows:



Systematic study has shown that the reaction is applicable not only to methyl ethyl ketone, but also to *cyclo*hexanone and its 3- and 4-methyl derivatives. A wide variety of substituted aniline derivatives has also been successfully used. **2 : 3-Dimethylquinoline, 2 : 3-dimethyl-7 : 8-benzoquinoline, and 2 : 3-*dimethyl*-5 : 6-*benzoquinoline*** have been synthesised from formyl methyl ethyl ketone and aniline, 1-naphthylamine, and 2-naphthylamine respectively. The same amines and formyl*cyclo*hexanone yielded, by way of the corresponding anils, **1 : 2 : 3 : 4-tetrahydroacridine, 6 : 7 : 8 : 9-*tetrahydro*-1 : 2-*benzacridine*,** and **6 : 7 : 8 : 9-tetrahydro-3 : 4-benzacridine** respectively. The constitution of the last two compounds was established by dehydrogenation with selenium to 1 : 2-benzacridine and 3 : 4-benzacridine respectively.

An interesting feature of the synthesis is the apparent formation of only one isomeride from *m*-substituted anilines where two isomerides are theoretically to be expected. It has been possible to determine whether the methyltetrahydroacridine obtained from *m*-toluidine is the 6- or the 8-substituted derivative. The formyl derivative of 3-methyl*cyclo*hexanone (IV) (Wallach and Steindorff, *Annalen*, 1903, **329**, 109) was condensed with aniline to give 2-methyl-1 : 2 : 3 : 4-tetrahydroacridine (III), apparently identical with the compound obtained by Borsche (1910, *loc. cit.*) from 3-methyl*cyclo*hexanone by the isatin method. This base gave 2-methylacridine (V) on dehydrogenation with selenium, identical with the dehydrogenation product of the methyltetrahydroacridine obtained from formyl*cyclo*hexanone (I) and *m*-toluidine. This compound has therefore been assigned the constitution of **8-*methyl*-1 : 2 : 3 : 4-*tetrahydroacridine*** (II).



(I.) (II.) (V.) (III.) (IV.)

Experimental.

Corrected m. p.'s given throughout. Microanalyses are by Mr. R. Maxim, University Chemical Laboratories, Cambridge.

Formyl*cyclo*hexanone was prepared essentially according to the directions of Borsche (1910, *loc. cit*): Sodium wire (23 g.), suspended in dry ether (500 ml.), was treated with a mixture of *cyclo*hexanone (110 ml.) and amyl formate (140 ml.), added dropwise under reflux during 1 hour with occasional shaking. After 12 hours the mixture was treated with 500 ml. of ice-water, the aqueous layer extracted with ether, and the formyl*cyclo*hexanone liberated from the sodium salt by acidification with cold dilute hydrochloric acid. It was extracted with ether and distilled, b. p. 86—88°/14 mm. Yield, 76 g.

Formyl methyl ethyl ketone (cf. Diels and Ilberg, *Ber.*, 1916, **49**, 158) was prepared by treating dry sodium ethoxide (from 10·6 g. of sodium), suspended in ether (330 ml.), at 0° with a mixture of methyl ethyl ketone (33 g.) and amyl

formate (54 g.). After 24 hours at 0° the sodium salt was collected, washed with ether, dried, and either used directly or dissolved in water and the formyl derivative liberated with ice-cold dilute sulphuric acid.

The anils were in general prepared by condensation of equivalent amounts of formyl methyl ethyl ketone or formyl-*cyclo*hexanone and the appropriate amine, both in alcoholic solution.

The following general procedure was used for the synthesis of the dialkylquinolines : The anil (1 mol.) in 10—20 vols. of absolute alcohol, amine hydrochloride (1 mol.), and anhydrous zinc chloride (1 mol.) were refluxed for 8—12 hours. The mixture was then made alkaline, and the basic portion extracted with ether. The dialkylquinoline was isolated from the residue left on removal of the ether by fractional ditillation under reduced pressure, or in a few cases as the picrate, and was purified by crystallisation from light petroleum or from aqueous acetone, yield, 50%. The picrates were all prepared in alcoholic solution and formed yellow crystals which were purified from nitrobenzene or from alcohol.

2 : 3-Dimethylquinoline, needles, m. p. 68—69° (Found : C, 84·3; H, 6·8; N, 9·2. Calc. : C, 84·1; H, 7·0; N, 8·9%) [picrate, m. p. 228—229° (decomp.) (Found : N, 14·5. Calc. : N, 14·5%)], was prepared from 3-(phenyliminomethyl)-butan-2-one (Diels and Ilberg, *Ber.*, 1916, **49**, 158). Pfitzinger (*J. pr. Chem.*, 1897, **56**, 315) gives m. p. 68—69° and 229° respectively.

2 : 3-*Dimethyl*-5 : 6-*benzoquinoline*, flat needles, m. p. 124—125° (Found : C, 86·7; H, 6·2; N, 7·0. $C_{15}H_{13}N$ requires C, 87·0; H, 6·3; N, 6·8%) [*picrate*, m. p. 260—261° decomp. (Found : N, 11·9. $C_{15}H_{13}N,C_6H_3O_7N_3$ requires N, 12·8%)], was prepared from 3-(*β-naphthyliminomethyl*)*butan*-2-*one*, pale yellow needles, m. p. 171—172° (Found : C, 79·9; H, 6·6; N, 6·2. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%). 2 : 3-Dimethyl-7 : 8-benzoquinoline, plates, m. p. 86—87° (Found : C, 86·8; H, 6·5; N, 7·0. Calc. : C, 87·0; H, 6·3; N, 6·8%) [picrate, m. p. 233·5° (decomp.) (Found : N, 12·5. Calc. : N, 12·8%)], was prepared from 3-(*α-naphthyliminomethyl*)*butan*-2-*one*, yellow needles, m. p. 110—111° (Found : C, 80·3; H, 6·8; N, 6·5. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%). Schenck and Bailey (*J. Amer. Chem. Soc.*, 1941, **63**, 2331) give m. p. 83—84° and 228—229° respectively.

1 : 2 : 3 : 4-Tetrahydroacridine formed prisms, m. p. 55—56° (Found : C, 85·0; H, 7·0; N, 7·9. Calc. : C, 85·2; H, 6·7; N, 7·7%), and its picrate had m. p. 222° (decomp.) (Found : N, 13·4. Calc. : N, 13·6%), neither depressed by authentic specimens prepared by Borsche's method (*Ber.*, 1908, **41**, 2203).

6 : 7 : 8 : 9-*Tetrahydro*-1 : 2-*benzdcridine*, prisms, m. p. 96·5—97·5°, b. p. 254°/18 mm. (Found : C, 87·5; H, 6·6; N, 5·8. $C_{17}H_{15}N$ requires C, 87·6; H, 6·4; N, 6·0%) [*picrate*, m. p. 210·5—211·5° (decomp.) (Found : N, 12·4. $C_{17}H_{15}N,C_6H_3O_7N_3$ requires N, 12·1%)], was prepared from 1-(*α-naphthyliminomethyl*)cyclo*hexan*-2-*one*, orange crystals, m. p. 118—119° (Found : C, 80·8; H, 6·9; N, 5·6. $C_{17}H_{17}ON$ requires C, 81·2; H, 6·8; N, 5·6%). 1 : 2-Benzacridine, m. p. 108° (Found : C, 88·8; H, 5·0; N, 6·3. Calc. : C, 89·1; H, 4·8; N, 6·1%) [picrate, m. p. 229—230° (decomp.) (Found : N, 12·5. Calc. : N, 12·2%)], was obtained on dehydrogenation with selenium; Ullmann and Le Torre (*Ber.*, 1904, **37**, 2922) give m. p. 108° and 226—229° respectively. 6 : 7 : 8 : 9-Tetrahydro-3 : 4-benzacridine, plates, m. p. 115—116°, b. p. 260°/18 mm. (Found : C, 87·4; H, 6·6; N, 6·1. Calc. : C, 87·6; H, 6·4; N, 6·0%) [picrate, m. p. 219—220° (decomp.) (Found : N, 12·5. Calc. : N, 12·1%)], identical with the base, m. p. 114—115° (picrate, m. p. 218—219°), formulated by Kenner, Ritchie, and Wain (J., 1937, 1526) as tetrahydrobenzphenanthridine, was prepared from 1-(*β-naphthyliminomethyl*)cyclo*hexan*-2-*one*, pale yellow needles, m. p. 181—182° (Found : C, 81·1; H, 6·8; N, 5·8. $C_{17}H_{17}ON$ requires C, 81·2; H, 6·8; N, 5·6%). On dehydrogenation the base gave 3 : 4-benzacridine, m. p. 131° (Found : C, 89·2; H, 4·7; N, 6·2. Calc. : C, 89·1; H, 4·8; N, 6·1%) [picrate, m. p. 265—266° (decomp.) (Found : N, 12·4. Calc. : N, 12·2%)], not depressed by authentic specimens prepared by Ullmann's method (D.R.-P. 123,260).

9-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridine* formed octahedra, m. p. 77—78°, b. p. 190°/20 mm. (Found : C, 85·0; H, 7·5; N, 7·3. $C_{14}H_{15}N$ requires C, 85·3; H, 7·6; N, 7·1%); the *picrate* had m. p. 215—216° (decomp.) (Found : N, 13·0. $C_{14}H_{15}N,C_6H_3O_7N_3$ requires N, 13·1%). 8-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridine*, prismatic needles, m. p. 100—101°, b. p. 208°/25 mm. (Found : C, 85·6; H, 7·7; N, 7·4%) [*picrate*, m. p. 189—190° (decomp.) (Found : N, 12·8%)], was prepared from 1-(m-*tolyliminomethyl*)cyclo*hexan*-2-*one*, yellow needles, m. p. 152—153° (Found : C, 78·3; H, 8·2; N, 6·7. $C_{14}H_{17}ON$ requires C, 78·1; H, 7·9; N, 6·5%), and was dehydrogenated to 2-methylacridine, m. p. 129—130° (Found : C, 87·3; H, 6·0; N, 7·5. Calc. : C, 87·0; H, 5·7 : N, 7·3%) [*picrate*, m. p. 225—226° (decomp.) (Found : N, 13·0. $C_{14}H_{11}N,C_6H_3O_7N_3$ requires N, 13·3%)], for which Borsche (*Annalen*, 1910, **377**, 117) gives m. p. **125—126°**. 7-*Methyl*-1 : 2 : 3 : 4-*tetrahydroacridine*, octahedra, m. p. 61—62° (Found : C, 85·6; H, 7·7; N, 7·1%) [*picrate*, m. p. 189·5—190·5° (decomp.) (Found : N, 13·0%)], was prepared from 1-(p-*tolyliminomethyl*)cyclo*hexan*-2-*one*; feathery yellow crystals, m. p. 163—164° (Found : C, 78·4; H, 8·1; N, 6·7%). 2-Methyl-1 : 2 : 3 : 4-tetrahydroacridine, octahedra, m. p. 76—77°, b. p. 195°/15 mm. (Found : C, 85·2; H, 7·6; N, 7·5%) [*picrate*, m. p. 184—185° (decomp.) (Found : N, 12·3%)], was dehydrogenated to 2-methylacridine, m. p. 129—130° (Found : C, 87·1; H, 6·0; N, 7·3%) [picrate, m. p. 225—226° (decomp.) (Found : N, 13·4%)]. Both base and picrate are identical with the compounds described under 8-methyl-1 : 2 : 3 : 4-tetrahydroacridine. 3-Methyl-1 : 2 : 3 : 4-tetrahydroacridine, octahedra, m. p. 87—88°, b. p. 180°/15 mm. (Found : C, 85·2; H, 7·4; N, 7·3%) [picrate, m. p. 199—200° (decomp.) (Found : N, 12·8%)], was prepared from 1-(*phenyliminomethyl*)-4-*methyl*cyclo*hexan*-2-*one*, orange-yellow plates, m. p. 161—162° (Found : C, 78·0; H, 7·8; N, 6·8. $C_{14}H_{17}ON$ requires C, 78·1; H, 7·9; N, 6·5%); Borsche (*loc. cit.*) gives m. p. 84—85° and 194—195° respectively.

6 : 9-*Dimethyl*-1 : 2 : 3 : 4-*tetrahydroacridine*, prisms, m. p. 38—39° (Found : C, 85·5; H, 8·3; N, 6·7. $C_{15}H_{17}N$ requires C, 85·3; H, 8·1; N, 6·6%) [*picrate*, m. p. 187—188° (decomp.) (Found : N, 12·4. $C_{15}H_{17}N,C_6H_3O_7N_3$ requires N, 12·7%)], was prepared from 1-p-*xylyliminomethyl*)cyclo*hexan*-2-*one*, orange-yellow plates, m. p. 100—101° (Found : C, 78·3; H, 8·1; N, 6·5. $C_{15}H_{19}ON$ requires C, 78·6; H, 8·3; N, 6·1%).

7-*Phenyl*-1 : 2 : 3 : 4-*tetrahydroacridine*, needles, m. p. 130° (Found : C, 88·3; H, 6·7; N, 5·5. $C_{19}H_{17}N$ requires C, 88·0; H, 6·6; N, 5·4%) [*picrate*, m. p. 246—247° (decomp.) (Found : N, 11·3. $C_{19}H_{17}N,C_6H_3O_7N_3$ requires N, 11·5%)], was prepared from 1-(*diphenylyl*-4′-*iminomethyl*)cyclo*hexan*-2-*one*, yellow needles, m. p. 201—202° (Found : C, 82·2; H, 7·0; N, 5·2. $C_{19}H_{19}ON$ requires C, 82·3; H, 6·9; N, 5·1%). It was dehydrogenated to 3-*phenylacridine*, plates, m. p. 127—128° (Found : C, 89·3; H, 5·4; N, 5·6. $C_{19}H_{13}N$ requires C, 89·4; H, 5·1; N, 5·5%), of which the *picrate* had m. p. 244—245° (decomp.) (Found : N, 11·5. $C_{19}H_{13}N,C_6H_3O_7N_3$ requires N, 11·6%).

9-*Chloro*-1 : 2 : 3 : 4-*tetrahydroacridine* formed octahedra, m. p. 94·5—95·5°, b. p. 220°/20 mm. (Found : C, 71·4; H, 5·8; N, 6·6. $C_{13}H_{12}NCl$ requires C, 71·7; H, 5·5; N, 6·4%); the *picrate* had m. p. 197—198° (decomp.) (Found : N, 12·6. $C_{13}H_{12}NCl,C_6H_3O_7N_3$ requires N, 12·8%). 6(or 8)-*Chloro*-1 : 2 : 3 : 4-*tetrahydroacridine*, octahedra, m. p. 92°, b. p. 202—203°/15 mm. (Found : C, 71·3; H, 5·6; N, 6·8%) [*picrate*, m. p. 204—205° (decomp.) (Found : N, 12·6%)], was prepared from 1-(m-*chlorophenyliminomethyl*)cyclo*hexan*-2-*one*, lemon-yellow needles, m. p. 148—150° (Found : C, 66·9; H, 6·3; N, 6·3. $C_{13}H_{14}ONCl$ requires C, 66·4; H, 6·0; N, 6·0%). 7-*Chloro*-1 : 2 : 3 : 4-*tetrahydroacridine*, flat needles, m. p. 95—96°, b. p. 212—214°/20 mm. (Found : C, 72·0; H, 5·6; N, 6·6%) [*picrate*, m. p. 188—189° (decomp.). (Found : N, 12·8%)], was prepared from 1-(p-*chlorophenyliminomethyl*)cyclo*hexan*-2-*one*, lemon-yellow octahedra, m. p. 169—170° (Found : C, 66·3; H, 5·8; N, 6·2%).

9-*Bromo*-1 : 2 : 3 : 4-*tetrahydroacridine* formed octahedra, m. p. 79—80°, b. p. 227—228°/15 mm. (Found : C, 59·3; H, 4·8; N, 5·4. $C_{13}H_{12}NBr$ requires C, 59·5; H, 4·6; N, 5·3%) [*picrate*, m. p. 191—192° (decomp.) (Found : N, 11·4. $C_{13}H_{12}NBr,C_6H_3O_7N_3$ requires N, 11·1%)]. 6(or 8)-*Bromo*-1 : 2 : 3 : 4-*tetrahydroacridine*, needles, m. p. 86—87°, b. p. 217—218°/15 mm. (Found : C, 59·7; H, 4·7; N, 5·4%) [*picrate*, m. p. 213·5—214·5° (decomp.) (Found : N, 11·5%)],

was prepared from 1-(m-*bromophenyliminomethyl*)cyclo*hexan*-2-*one*, lemon-yellow plates, m. p. 155—156° (Found: C, 55·3; H, 5·3; N, 5·3. $C_{13}H_{14}ONBr$ requires C, 55·7; H, 5·0; N, 5·0%). 7-Bromo-1 : 2 : 3 : 4-tetrahydroacridine, octahedra, m. p. 93—94°, b. p. 223—224°/18 mm. (Found: C, 59·6; H, 4·8; N, 5·4%) [picrate, m. p. 213·5—214·5° (decomp.) (Found: N, 11·4%)], was prepared from 1-(p-*bromophenyliminomethyl*)cyclo*hexan*-2-*one*, corn-coloured plates, m. p. 175—176° (Found: C, 55·7; H, 5·2; N, 5·3%); Borsche (*loc. cit.*) gives m. p. 94° and 195° respectively.

7-*Iodo*-1 : 2 : 3 : 4-*tetrahydroacridine* (4 hrs. refluxing, no zinc chloride), squat rods, m. p. 86·5—87·5° (Found: C, 50·5; H, 4·2; N, 4·6. $C_{13}H_{12}NI$ requires C, 50·5; H, 3·9; N, 4·5%) [*picrate*, m. p. 219·5—220·5° (decomp.) (Found: N, 10·1. $C_{13}H_{12}NI,C_6H_3O_7N_3$ requires N, 10·4%)], was prepared from 1-(p-*iodophenyliminomethyl*)cyclo*hexan*-2-*one*, lemon-yellow needles, m. p. 168—169° (Found: C, 47·9; H, 4·3; N, 4·6. $C_{13}H_{14}ONI$ requires C, 47·7; H, 4·3; N, 4·3%).

6(or 8)-*Carbethoxy*-1 : 2 : 3 : 4-*tetrahydroacridine*, needles, m. p. 63—64° (Found: C, 75·3; H, 6·5; N, 5·5. $C_{16}H_{17}O_2N$ requires C, 75·3; H, 6·7; N, 5·5%) [*picrate*, m. p. 161° (decomp.) (Found: N, 11·0. $C_{16}H_{17}O_2N,C_6H_3O_7N_3$ requires N, 11·1%)], was prepared from 1-(m-*carbethoxyphenyliminomethyl*)cyclo*hexan*-2-*one*, flat yellow needles, m. p. 143—144° (Found: C, 70·0; H, 7·2; N, 5·4. $C_{16}H_{19}O_3N$ requires C, 70·3; H, 7·0; N, 5·1%). 7-*Carbethoxy*-1 : 2 : 3 : 4-*tetrahydroacridine*, prismatic needles, m. p. 94·5—95·5°, b. p. 234°/20 mm. (Found: C, 75·4; H, 6·7; N, 5·8%) [*picrate*, m. p. 197—198° (decomp.) (Found: N, 11·0%)], was prepared from 1-(p-*carbethoxyphenyliminomethyl*)cyclo*hexan*-2-*one*, feathery yellow needles, m. p. 181—182° (Found: C, 70·6; H, 7·0; N, 5·3%). It was hydrolysed to 1 : 2 : 3 : 4-*tetrahydroacridine*-7-*carboxylic acid*, needles, m. p. 290—291° (Found: C, 74·4; H, 5·7; N, 6·4. $C_{14}H_{13}O_2N$ requires C, 74·0; H, 5·7; N, 6·1%). Acridine derivatives could not be obtained from 1-(o-*carboxyphenyliminomethyl*)cyclo*hexan*-2-*one*, orange-yellow needles, m. p. 199—200° (Found: C, 68·8; H, 6·0; N, 5·4. $C_{14}H_{15}O_3N$ requires C, 68·5; H, 6·1; N, 5·7%), and from 1-(o-*carbomethoxyphenyliminomethyl*)cyclo*hexan*-2-*one*, needles, m. p. 134·5—135·5° (Found: C, 69·6; H, 6·3; N, 5·6. $C_{15}H_{17}O_3N$ requires C, 69·5; H, 6·6; N, 5·4%).

7-*Hydroxy*-1 : 2 : 3 : 4-*tetrahydroacridine*, plates, m. p. 290—291° (Found: C, 78·8; H, 6·7; N, 7·4. $C_{13}H_{13}ON$ requires C, 78·4; H, 6·5; N, 7·0%) [*picrate*, m. p. 229·5—230·5° (decomp.) (Found: N, 12·5. $C_{13}H_{13}ON,C_6H_3O_7N_3$ requires N, 13·1%)], was prepared from 1-(p-*hydroxyphenyliminomethyl*)cyclo*hexan*-2-*one*, golden-yellow plates, m. p. 154—155° (Found: C, 71·7; H, 7·0; N, 6·7. $C_{13}H_{15}O_2N$ requires C, 71·9; H, 6·9; N, 6·5%).

7-*Nitro*-1 : 2 : 3 : 4-*tetrahydroacridine*.—1-(p-*Nitrophenyliminomethyl*)cyclo*hexan*-2-*one* (40 g.), yellow needles, m. p. 244—245° (Found: C, 63·4; H, 5·9; N, 11·5. $C_{13}H_{14}O_3N_2$ requires C, 63·4; H, 5·7; N, 11·4%), was treated as above, and the mixture poured into excess of sodium carbonate solution and extracted with benzene (1000 ml.). The product in dry benzene (300 ml.) was refluxed for 30 minutes with acetic anhydride (50 ml.), water added (700 ml.), and the *p*-nitroacetanilide collected after 12 hours and washed three times with benzene (100 ml.). The acetic acid layer was removed, and the benzene washed with small volumes of dilute hydrochloric acid (total, 2 l. containing 700 ml. of concentrated acid). The acetic acid and the hydrochloric acid liquors were bulked and made alkaline with ammonia; the precipitated 7-*nitro*-1 : 2 : 3 : 4-*tetrahydroacridine* crystallised from acetone (norit) in needles (15 g.), m. p. 170·5—171·5° (Found: C, 68·6; H, 5·3; N, 12·5. $C_{13}H_{12}O_2N_2$ requires C, 68·4; H, 5·3; N, 12·3%). The *picrate* had m. p. 204·5° (decomp.) (Found: N, 14·9. $C_{13}H_{12}O_2N_2,C_6H_3O_7N_3$ requires N, 15·3%).

On reduction 7-*amino*-1 : 2 : 3 : 4-*tetrahydroacridine* was obtained; it formed rods, m. p. 141° (Found: C, 79·0; H, 7·2; N, 14·4. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1; N, 14·4%), and gave an *acetyl* derivative crystallising in needles, m. p. 218·5—219·5° (Found: C, 75·1; H, 7·0; N, 11·9. $C_{15}H_{16}ON_2$ requires C, 75·0; H, 6·7; N, 11·7%). An acridine derivative could not be obtained from 1-(m-*nitrophenyliminomethyl*)cyclo*hexan*-2-*one*, orange needles, m. p. 171—172° (Found: C, 63·4; H, 6·0; N, 11·6%).

9-*Methoxy*-1 : 2 : 3 : 4-*tetrahydroacridine*, octahedra, m. p. 121·5—122·5°, b. p. 212°/20 mm. (Found: C, 79·0; H, 7·1; N, 7·0. $C_{14}H_{15}ON$ requires C, 78·9; H, 7·0; N 6·6%) [*picrate*, m. p. 206·5—207·5° (decomp.) (Found: N, 12·7. $C_{14}H_{15}ON,C_6H_3O_7N_3$ requires N, 12·7%)], was prepared from 1-(o-*methoxyphenyliminomethyl*)cyclo*hexan*-2-*one*, feathery yellow needles, m. p. 131—132° (Found: C, 72·8; H, 7·6; N, 6·2. $C_{14}H_{17}O_2N$ requires C, 72·7; H, 7·4; N, 6·1%). 7-*Methoxy*-1 : 2 : 3 : 4-*tetrahydroacridine*, octahedra, m. p. 90—91°, b. p. 223°/15 mm. (Found: C, 79·1; H, 7·3; N, 6·7%) [*picrate*, m. p. 223·5—224·5° (decomp.) (Found: N, 11·7%)], was prepared from 1-(p-*methoxyphenyliminomethyl*)cyclo*hexan*-2-*one*, pale yellow needles, m. p. 149—150° (Found: C, 72·9; H, 7·6; N, 6·3%).

6(or 8)-*Acetyl*-1 : 2 : 3 : 4-*tetrahydroacridine*, flat needles, m. p. 131—132° (Found: C, 79·9; H, 6·5; N, 6·2. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%) [*picrate*, m. p. 211—212° (decomp.) (Found: N, 11·8. $C_{15}H_{15}ON,C_6H_3O_7N_3$ requires N, 12·3%)], was prepared from 1-(m-*acetylphenyliminomethyl*)cyclo*hexan*-2-*one*, feathery yellow crystals, m. p. 139—140° (Found: C, 74·0; H, 7·3; N, 6·0. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·0; N, 5·8%).

7-*Phenylamino*-1 : 2 : 3 : 4-*tetrahydroacridine*, golden-yellow needles, m. p. 173°, b. p. 290°/15 mm. (Found: C, 83·1; H, 6·9; N, 10·2. $C_{19}H_{18}N_2$ requires C, 83·2; H, 6·6; N, 10·2%) [*picrate*, orange-brown needles, m. p. 251—252° (decomp.) (Found: N, 13·7. $C_{19}H_{18}N_2,C_6H_3O_7N_3$ requires N, 13·9%)], was prepared from 1-(p-*phenylaminophenyliminomethyl*)cyclo*hexan*-2-*one*, golden-yellow plates, m. p. 144—145° (Found: C, 78·6; H, 7·4; N, 10·0. $C_{19}H_{20}ON_2$ requires C, 78·1; H, 6·9; N, 9·6%).

Quinoline derivatives could not be obtained from the formyl derivatives of the following ketones: Acetophenone, propiophenone, benzyl methyl ketone, phenyl benzyl ketone, *cyclo*pentanone, *i*-menthone, 2-methyl*cyclo*hexanone, α-tetralone, and acetoacetic ester. 2-Hydroxy-1-naphthaldehyde anil was recovered unchanged.

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148. *Resemblance between Surface Films on Solids and on Water.*

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As Bangham has shown, the quantities FA and FS can be calculated for the adsorbed film of a gas on a solid from the adsorption isotherm by integration of the Gibbs adsorption equation (F = surface pressure of the adsorbed film, A = area occupied per adsorbed molecule, S = "specific surface" of the adsorbent, *i.e.*, its adsorbing area per g.). Curves of FA against FS, now drawn from published isotherms, exhibit close correspondence to surface films on water: the film states gaseous (G), liquid-expanded (L_1), liquid-condensed (L_2), and the intermediate state (I) between L_1 and L_2 have their counterparts in gas–solid adsorption. From the slope

of the *FA–FS* curve where it becomes linear, both the adsorbing area *S* and the monolayer capacity of the adsorbent (the number of molecules it can take up per g. in a completed monolayer) can be calculated.

Formation of layers more than one molecule thick sometimes occurs, but is not to be associated with the characteristic loops often obtained in the adsorption isotherms of vapours on gels; the *FA–FS* curves in the latter cases show that the adsorbed layer remains unimolecular throughout the region covered by the loop, and that the hysteresis orginates, not in capillary condensation, but in the transformation of state $L_1 \rightleftharpoons I \rightleftharpoons L_2$ occurring within the *monolayer*.

In van der Waals adsorption of a gas on a solid, the molecules in the adsorbed layer are frequently mobile on the surface, and consequently produce a two-dimensional pressure *F* analogous to the surface pressure of films on water. Two-dimensional equations of state relating *F* to the area *A* (see above) have been derived, *e.g.*, by Volmer (*Z. physikal. Chem.*, 1925, **115**, 253), Kar (*Physikal. Z.*, 1925, **26**, 615), and Bradley (*Phil. Mag.*, 1929, **8**, 202; *Chem. Reviews*, 1937, **9**, 47); Langmuir (*J. Amer. Chem. Soc.*, 1932, **54**, 2798) further envisages the possible occurrence within the film of transformations of state resembling phase changes in bulk matter, and Fowler has demonstrated by statistical mechanics that the adsorbed film should break up into two phases under suitable conditions (*Proc. Camb. Phil. Soc.*, 1936, **32**, 144).

Experimental evidence for changes of state within the adsorbed layer on solids has been obtained by Bangham and his co-workers. Using the expansion of the adsorbent, which accompanies adsorption, as a measure of the surface pressure (Bangham and Fakhoury, J., 1931, 1324) and noting that the quantity adsorbed per g. of adsorbent is inversely proportional to *A*, they plotted curves of *FA* against λF (λ is a proportionality constant) for a number of gases and vapours adsorbed on charcoal. In one experiment, water vapour and ammonia gave curves very similar to the *pV–p* curves of an imperfect gas, and in another experiment with water vapour the *FA–F* graph closely resembled the *pV–p* curve of a vapour below its critical temperature, showing a region where two-dimensional condensation occurred at constant *F* (Bangham, Fakhoury, and Mohamed, *Proc. Roy. Soc.*, 1932, *A*, **138**, 177). With pyridine, benzene, and the lower primary alcohols, it was found that on standing, or better, on heating the charcoal in contact with the vapour and re-cooling ("annealing") the system, the values of *F* and *A* changed so that the *FA–F* graph took up a new, approximately linear, course, usually with a smaller slope (*loc. cit.*, p. 162); they interpreted this as a change of state from a "primary" to an "annealed" film (*ibid.*, 1934, *A*, **147**, 152), and directed attention to the similarity between the alcohol curves and the *FA–F* graphs calculable from Cassell and Salditt's data for the same substances adsorbed on liquid mercury (*Z. physikal. Chem.*, 1931, *A*, **155**, 299).

Later, Bangham (*Trans. Faraday Soc.*, 1937, **33**, 805) showed how to calculate the quantity *FS* from the adsorption-isotherm data alone, without recourse to expansion data, by integration of the Gibbs adsorption equation. Performing the integration graphically for Coolidge's data for water vapour adsorbed on sugar charcoal (*J. Amer. Chem. Soc.*, 1927, **49**, 713), Bangham and Razouk showed from the form of the *FA–F* graph (*S* being estimated by comparison with mercury adsorption) that two-dimensional condensation again occurred (*Trans. Faraday Soc.*, 1937, **33**, 1463).

The Gibbs equation has also been used by Palmer (*Proc. Roy. Soc.*, 1937, *A*, **160**, 254) to calculate *F* for benzene vapour adsorbed on a known area of vitreous silica, integration being performed algebraically; the resulting *FA–F* curve was similar to that for the liquid-expanded state of insoluble films on water.

It will now be shown that many other similarities appear between the states of films on water and on solids, when the data for gas–solid adsorption are set out as *FA–FS* curves, calculated by Bangham's procedure.

In order to facilitate this comparison, it is first necessary to summarise the *FA–F* graphs for the various states, and transformations of state, of films of insoluble substances on water. The states are those set out in the summary, the symbols being those of Harkins, Fraser, Young, and Boyd (*J. Chem. Physics*, 1940, **8**, 954; see also Harkins and Boyd, *J. Physical Chem.*, 1941, **45**, 20). The intermediate state I arises because the transition between the liquid-expanded and the liquid-condensed state, unlike that from the vaporous to the liquid-expanded, occurs over a definite range of values of *F* and not at one definite value. There is also a *solid* state, which could perhaps serve as an analogue of *immobile* adsorbed films on solids; it will not be considered here.

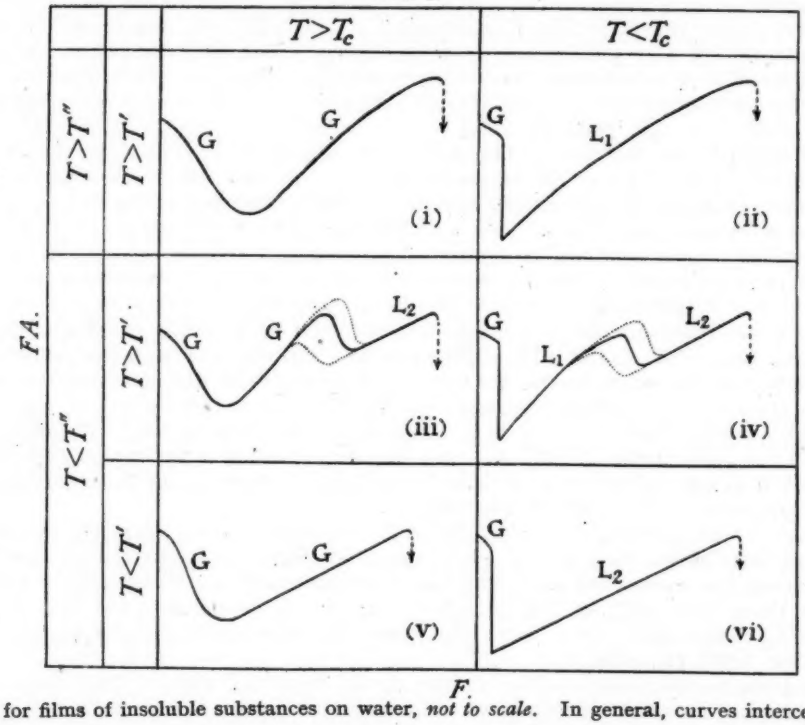
The *FA–F* curves are shown (not to scale) in Fig. 1. They can be derived from graphs given by Adam ("Physics and Chemistry of Surfaces," 1941, Chap. II), Harkins and Boyd (*loc. cit.*), or Dervichian (*J. Chem. Physics*, 1939, **7**, 931), or from the literature.

In Fig. 1, T_c is a temperature analogous to the critical temperature of liquefaction of a bulk fluid; T' and T'' also have the character of critical temperatures, but because of the experimental difficulty, or even impossibility, of working over a sufficiently wide range of temperature, it has not been possible hitherto to realise all six forms of the graph with any one substance. One cannot, therefore, say how far T_c, T', and T'' are to be regarded as constants characteristic of a given substance—*e.g.*, whether T_c would have the same value for the transition from diagram (v) to (vi) as from (i) to (ii); nor is the question of importance in the present connection, which is merely to show the possible types of curve and to indicate how they are related to their nearest neighbours. In any case, in view of the well-known sensitivity of film states to the ionic composition of the trough solution (*e.g.*, p_H and the concentration of metal ions), it is certain that T_c, T', and T'' could not be constant for a given adsorbate unless the ionic environment were constant.

The *slope*, *B*, of the *FA–F* graphs is of particular importance. Schofield and Rideal (*Proc. Roy. Soc.*, 1926, *A*, **110**, 167) pointed out that the slope of the curve where it becomes linear should be equal to the corresponding incompressible area A_0 of the adsorbed molecules, and they applied this relation to the gaseous state at high

surface pressure, and to the liquid-condensed state. In the latter state the value of B for long-chain compounds is usually *ca.* 19—20 A.^{2}. The detailed molecular structure of the film in this state is still in doubt, but it is agreed that the orientation of the molecules is either the same as, or very similar to, that in a sheet of molecules in the bulk crystal, the molecules being steeply, or even vertically, inclined to the water surface (Adam, *op. cit.*, p. 51; Alexander, *Proc. Roy. Soc.*, 1942, *A*, **179**, 486; Dervichian, *loc. cit.*, p. 945); Müller (*Proc. Roy. Soc.*, 1932, *A*, **138**, 514) states that the minimum area of cross-section of the hydrocarbon chain, perpendicular to its length, is 18·3 A.^{2}, and increases with temperature up to an average value of 19·5 A.^{2}. According to Langmuir

FIG. 1.



FA–F graphs for films of insoluble substances on water, *not to scale*. In general, curves intercept the *FA* axis at a value kT.

G = adsorbed gaseous (or vaporous) state; L_1 = liquid-expanded state; L_2 = liquid-condensed state; I = intermediate state between L_1 and L_2. The right-hand G branch of (i) and (ii) is indistinguishable in form from an L_1, and in (v) from an L_2, branch.

Broken line represents collapse of film, *i.e.*, transformation into a multimolecular layer. (Solid-condensed state, which may intervene between L_2 and collapse, omitted.)

Left-hand and right-hand dotted lines in (iii) and (iv) show curves for lower and higher temperatures respectively than the full line between them.

T_c = critical temperature; T' = temperature above which the L_2 state cannot occur; T'' = temperature below which the L_1 state cannot occur.

Experimental examples. There are numerous experimental results illustrating individual parts of the above curves, but the examples below have been chosen so as to cover as much as possible of the particular curve in a single experiment.

In the examples for (ii), (iii), (v), and (vi) the measurements were not carried as far as the collapse point.

Curve (i) $C_{14}H_{29}{\cdot}CO_2C_2H_5$ at 25°; Harkins and Boyd, *loc. cit.*
(ii) Myristic acid at 14·5°; Adam and Jessop, *Proc. Roy. Soc.*, 1926, *A*, **110**, 423.
(iii) Tridecyl methyl ketone at 12·5°; *idem*, *ibid.*, 1926, *A*, **112**, 362.
(iv) Pentadecoic acid at 27·5°; Harkins and Boyd, *loc. cit.*
(v) Nearest example $C_{16}H_{32}(CO_2Et)_2$ at 1°, where the right-hand branch is solid, not liquid-condensed; Adam and Jessop, *loc. cit.*, p. 376.
(vi) Ethyl stearate at 14°; Adam and Jessop, *ibid.*, 1926, *A*, **110**, 423.

(*J. Chem. Physics*, **1933**, **1**, 756) the adsorbed molecules in the L_2 state are aggregated into two-dimensional micelles. The *FA–F* curve for the gaseous state is concave to the F axis in its right-hand branch, so that the slope B, and consequently the incompressible area A_0, diminish as surface pressure increases in this region; at a given pressure the value of A_0 depends very much on the particular adsorbate; A_0 is always larger than the area characteristic of the liquid-condensed state (*e.g.*, for ethyl undecanedicarboxylate it is approx. 100 A.^{2}; Adam and Jessop, *Proc. Roy. Soc.*, 1926, *A*, **112**, 376) and it is generally agreed that in the gaseous state the molecules lie flat on the water surface (thus occupying a large area) except at high surface pressures, where they begin to tilt (Adam, *op. cit.*, p. 57).

The slope B for the liquid-expanded state also gradually diminishes as F increases, its value throughout

being greater than that for the liquid-condensed state, and less than that ordinarily obtained for the gaseous state; typical values are *ca.* 43 A.^{2} for pentadecoic acid on 0·01N-hydrochloric acid (Nutting and Harkins, *J. Amer. Chem. Soc.*, 1939, **61**, 1180) for the range $F = 0{\cdot}5$—$2{\cdot}0$ dynes/cm. and *ca.* 30 A.^{2} for the range 6—8 dynes/cm. It is clear that on the average the molecules of the film become progressively more steeply tilted as F increases, thus producing a gradually diminishing value of A_0. It is no longer possible to say, however, either for the L_1 state, or for the G state at higher pressures, that the slope of the FA–F curve at any point gives the exact value of A_0 at that point, for in deriving the relationship $B = A_0$ it is assumed that the attraction between the molecules in the film (due to a two-dimensional van der Waals's a) is independent of F, whereas in fact the gradual alteration in orientation cannot fail to change the interattraction, and that in a manner very difficult to predict. The slope should nevertheless give an approximate measure of A_0. The most widely accepted theory of the liquid-expanded state is Langmuir's theory of duplex films (*loc. cit.*), which is compatible with the idea that the molecules become progressively more steeply tilted as F increases.

The Adsorbed Film on Solids.—Gibbs's adsorption equation $\Gamma = (1/\boldsymbol{R}T)\mathrm{d}F/\mathrm{d}\log_e p$ may, as Bangham (*loc. cit.*) has shown, be integrated to

$$F = \boldsymbol{R}T\int_0^p \Gamma \mathrm{d}\log_e p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

Γ is the quantity adsorbed, in moles/sq. cm.; p is the equilibrium gas pressure in the free space.

Generally we are ignorant of the specific surface per g. of adsorbent, so only x, the number of molecules adsorbed per g. of asdorbent, *i.e.*, S sq. cm., can be measured. Since $\Gamma = x/\boldsymbol{N}S$, where $\boldsymbol{N}$ is Avogadro's number, $F = \boldsymbol{R}T\int_0^p (x/\boldsymbol{N}S)\mathrm{d}\log_e p$, *i.e.*,

$$FS = \boldsymbol{k}T\int_0^p x \mathrm{d}\log_e p \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $\boldsymbol{k}$ is the Boltzmann constant, $\boldsymbol{R}/\boldsymbol{N}$. The area per molecule, A, is S/x, so

$$FA = FS/x \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Following Bangham's procedure, FS will first be calculated by plotting x against $\log_e p$ and taking the area under the curve from zero up to any pressure p; FA is then found from (3), and plotted against FS.

Some difficulty arises in the graphical integration of $\int x \mathrm{d}\log_e p$ when, as is frequently the case, accurate measurements of adsorption are lacking at low pressures. Since $\log p$ becomes negative and infinite when $p = 0$, at one limit of integration, graphical integration becomes very uncertain. However, it is known that at sufficiently low pressures adsorption becomes very nearly proportional to the pressure. This relationship (analogous to Henry's law for the solubility of gases in liquids) provides a very easy means of integration, for when $x = mp$,

$$\int_0^{p_1} x \mathrm{d}\log_e p = mp_1 = x_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where x_1 is the value of x when $p = p_1$. Consequently, $FS = \boldsymbol{k}T\int_0^{p_1} x \mathrm{d}\log_e p = \boldsymbol{k}Tx_1$, *i.e.*, $FS/x_1 = \boldsymbol{k}T$, or from (3), $FA = \boldsymbol{k}T$.

This relationship between the Gibbs and the Henry equation was derived by Langmuir and applied to the adsorbed film of soluble substances at the surface of aqueous solutions (*J. Amer. Chem. Soc.*, 1917, **39**, 1888); he concluded that the film when very dilute acted as an ideal, two-dimensional gas. [As Langmuir pointed out, Traube (*Annalen*, 1891, **265**, 27) had already shown that the surface layer of dilute solutions obeyed a law analogous to Boyle's.] Langmuir and Kingdon reached a similar conclusion for very dilute films of cæsium vapour adsorbed on tungsten (*Proc. Roy. Soc.*, 1925, *A*, **106**, 61).

In gas–solid adsorption it may be that *exact* proportionality between x and p at low pressures obtains only if both adsorbent and adsorbate are particularly pure (Magnus and Kratz, *Z. anorg. Chem.*, 1929, **184**, 242); but ordinary cases of adsorption may be expected to approximate more or less closely to this, the film behaving *very nearly* as a two-dimensional perfect gas at low pressures. Every FA–FS graph may therefore be assumed to intersect the FA axis at or near the value $\boldsymbol{k}T$. Its detailed course for the region of low adsorptions can but rarely be mapped out, but in the range of high and medium adsorptions it is not much affected by uncertainties in the isotherm at low adsorptions, and so can still be drawn even if low-pressure data are scanty.

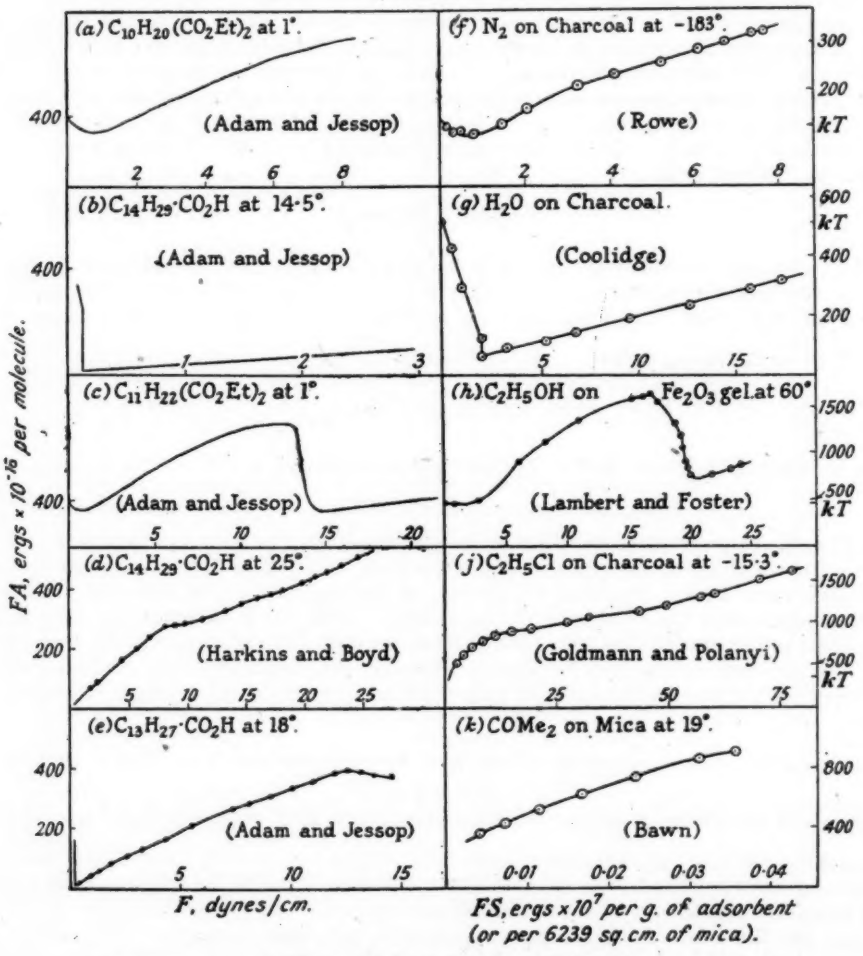
Numerous FA–FS graphs have been constructed from adsorption-isotherm data suitable for integration; examples and references are given in Figs. 2, 3, 4, and 5. In Fig. 2 there are given also the corresponding curves for insoluble films on water; the resemblance between the two sets of curves is striking, and leaves little doubt as to the similarity between adsorbed films on water and on solids.

One assumes that the extreme left-hand ends of curves (*j*) and (*k*) of Fig. 2 and of all the curves in Figs. 3, 4, and Fig. 5*a* are of the general form shown in (*a*) or (*b*) of Fig. 2, though much compressed along the FS axis. In Fig. 4*b*, branch YZ denotes the formation of a layer more than one molecule thick, as will be explained later.

The " imperfect gas " type of curve exemplified by Fig. 2*f* must always result from any adsorption isotherm which deviates slightly from Henry's law first in a " positive," then in a " negative " sense—*i.e.*, is first concave

then convex to the pressure axis. Several such cases are on record, but in all of them the deviations from $x = mp$ are small and possibly do not exceed experimental error (*e.g.*, hydrogen and nitrogen on charcoal at − 183°, Rowe, *Phil. Mag.*, 1926, **1**, 1042; hydrogen on charcoal at − 78°, Barrer and Rideal, *Proc. Roy. Soc.*, 1935, *A*, **149**, 240; nitrogen on sodium chloride at 18°, Durau, *Ann. Physik*, 1928, **87**, 307). More low-pressure data are required before it can be decided whether this behaviour exists or not.

FIG. 2.


(a) $C_{10}H_{20}(CO_2Et)_2$ at 1°.
(Adam and Jessop)
(b) $C_{14}H_{29}\cdot CO_2H$ at 14·5°.
(Adam and Jessop)
(c) $C_{11}H_{22}(CO_2Et)_2$ at 1°.
(Adam and Jessop)
(d) $C_{14}H_{29}\cdot CO_2H$ at 25°.
(Harkins and Boyd)
(e) $C_{13}H_{27}\cdot CO_2H$ at 18°.
(Adam and Jessop)
(f) N_2 on Charcoal at −183°.
(Rowe)
(g) H_2O on Charcoal.
(Coolidge)
(h) C_2H_5OH on Fe_2O_3 gel at 60°
(Lambert and Foster)
(j) C_2H_5Cl on Charcoal at −15·3°.
(Goldmann and Polanyi)
(k) $COMe_2$ on Mica at 19°.
(Bawn)
FA, ergs × 10⁻¹⁶ per molecule.
kT
F, dynes/cm.
FS, ergs × 10⁷ per g. of adsorbent (or per 6239 sq. cm. of mica).

References: (*a*), (*c*) *Proc. Roy. Soc.*, 1926, *A*, **112**, 376.
(*b*) *Ibid.*, 1926, *A*, **110**, 423.
(*d*) *J. Physical Chem.*, 1941, **45**, 21.
(*e*) *Proc. Roy. Soc.*, 1926, *A*, **112**, 364.
(*f*) *Phil. Mag.*, 1926, **1**, 1042.
(*g*), (*h*), (*j*) Ref. (12), Table, p. 701.
(*k*) *J. Amer. Chem. Soc.*, 1932, **54**, 77.

The existence of a " hydrogen type " of gaseous film is more certain. The *FA*–*FS* curves for this state (which does not seem to be represented amongst films on water) rise steadily from the value $FA = kT$ at $F = 0$ and soon become linear; an example is provided by Langmuir's data for carbon dioxide adsorbed on mica at − 118° (*J. Amer. Chem. Soc.*, 1918, **40**, 1361). The Langmuir adsorption equation, $x = k_1k_2p/(1 + k_2p)$, where k_1 and k_2 are constants, gives rise to a curve similar to the hydrogen type: on integration, we have $FA = -(k_1/x)\log_e(1 - x/k_1)$ and $FS = -k_1\log_e(1 - x/k_1)$, and on plotting FA against FS a curve rising steadily from its intercept with the FA axis at kT, and slightly convex to the FS axis, is obtained. Its slope becomes nearly constant as $x/k_1 \to 1$, and for the range $x/k_1 = 0{\cdot}90$—$0{\cdot}95$ it is approx. $1{\cdot}2k_1$. [The relationship between the Gibbs and the Langmuir equation has been discussed by Innes and Rowley (*J. Physical Chem.*, 1941, **45**, 158), who derive an expression for F in terms of A and A_0, also for FA in terms of x, though not of F.]

Fig. 2*g*, for water vapour on charcoal (Coolidge, *loc. cit.*), is very similar in shape to the curve given by Bangham and Razouk (*loc. cit.*) (see p. 697). The vertical branch, denoting condensation from a G to an L_2 film, results from an isotherm having a region where p remains constant whilst x increases; this behaviour is rare

and may even be confined to the water–charcoal system, for no other examples of the phenomenon can be traced.

Systems corresponding to type (iii) *or* (iv) *of Fig.* 1.

Adsorbent.	Temp.	Adsorbate.	Monolayer capacity, c.c. (N.T.P.) per g.	Ref.	Fig. No.
NaCl	−183°	NO	—	1	4*a*
Mica	35	C_6H_6	—	2	—
Glass	0	C_6H_5Me	—	3	—
Casein	—	NH_3	26 ± 2	4	—
Fe_2O_3 gel ...	40	C_6H_6	69 ± 2	5	5*a*
,, ...	60	EtOH	76 ± 5	6	2*h*
SiO_2 gel	60	H_2O	292 ± 15	7	—
,, ...	*ca.* 15	H_2O	840 ± 15	8	—
Charcoal.....	30	CO_2	147 ± 5	9	—
,, ...	0	CO_2	150 ± 5	,,	3*b*
,, ...	−76	CO_2	145 ± 5	,,	—
*Charcoal I	0	CO_2	152 ± 8	10	3*a*
,,	,,	C_2H_2	123 ± 5	,,	3*d*
,,	,,	C_2H_4	98 ± 10	,,	3*c*
,,	,,	C_2H_6	90 ± 10	,,	—
*Charcoal I...	0°	N_2O	140 ± 5	10	—
,, ...	,,	SO_2	112 ± 12	,,	—
*Charcoal II	,,	N_2O	145 ± 15	,,	—
,,	,,	SO_2	120 ± 10	,,	—
*Charcoal I...	40·3	SO_2	105 ± 10	,,	—
Charcoal ...	0	EtCl	208 ± 15	11	—
,, ...	−15·3	EtCl	226 ± 15	,,	2*j*
,, ...	20·5	CS_2	305 ± 10	,,	—
† ,, ...	0	H_2O	218 ± 5	12	2*g*
,, ...	147	C_6H_6	185 ± 10	,,	—
,, Xb	0	SO_2	135 ± 3	13	—
,, Xc	,,	SO_2	136 ± 3	,,	—
,, Xa	,,	SO_2	119 ± 3	,,	4*c*
,, XIIb	,,	EtCl	47 ± 2	,,	4*b*

* In these cases the "intermediate" region I is only just detectable. The low-pressure end of the *FA–FS* curve is somewhat doubtful (owing to paucity of low-pressure isotherm data) and it is just possible that the curves may be of the "hydrogen" type. The slope of the right-hand end, and therefore the value of the monolayer capacity, would scarcely be altered if this were so.

† This is comparable to type (vi), Fig. 1.

References. [1] Tomkins, *Trans. Faraday Soc.*, 1936, **32**, 643. [2] Bangham and Mosallam, *Proc. Roy. Soc.*, 1938, *A*, **166**, 558. [3] Carver, *J. Amer. Chem. Soc.*, 1923, **45**, 63. [4] Bancroft and Barnett, *J. Physical Chem.*, 1930, **34**, 489. [5] Lambert and Clark, *Proc. Roy. Soc.*, 1929, *A*, **122**, 505. [6] Lambert and Foster, *ibid.*, 1932, *A*, **136**, 367. [7] *Idem* (Expt. 7), *ibid.*, 1931, *A*, **134**, 246. [8] Anderson, *Z. physikal. Chem.*, 1914, **88**, 191. [9] Titoff, *ibid.*, 1910, **74**, 650. [10] Gregg, J., 1927, 1494. [11] Goldmann and Polanyi, *Z. physikal. Chem.*, 1928, **132**, 321. [12] Coolidge, *loc. cit.* [13] Gregg, to be published.

Much the commonest kind of curve appears to be that corresponding to curves (iii) and (iv) of Fig. 1 (see Figs. 2*h*, 2*j*; 3, 4, and 5*a*; also table). Owing to the lack of low-pressure data it is not usually possible to assign a given curve definitely to one or other of these classes, *i.e.*, to say whether it is G–I–L_2 or G–L_1–I–L_2. Fig. 2*h* represents a G–I–L_2 curve of an uncommon type, in that the perfect-gas behaviour appears to persist up to higher pressures than usually; the initial flat branch, however, depends on three experimental points only, and if more were available the curve might fall in line with either (iii) or (iv) of Fig. 1.

The degree of prominence of the intermediate region I differs considerably from one curve to another, and frequently the L_1 branch passes almost imperceptibly into the L_2. Similar diversity in this respect is found amongst films on water, where *FA–F* graphs are known corresponding to successive stages from the almost vertical I branch of Fig. 2*c* to the scarcely perceptible I region of Fig. 2*d*, the prominence of the I region being controlled for films on water by various factors, notably temperature and molecular structure.

Acetone on mica (Fig. 2*h*) is compared with a liquid-expanded film on water (Fig. 2*e*), but if we had enough low-pressure data it might prove to be comparable with a *gaseous* film at high surface pressure.

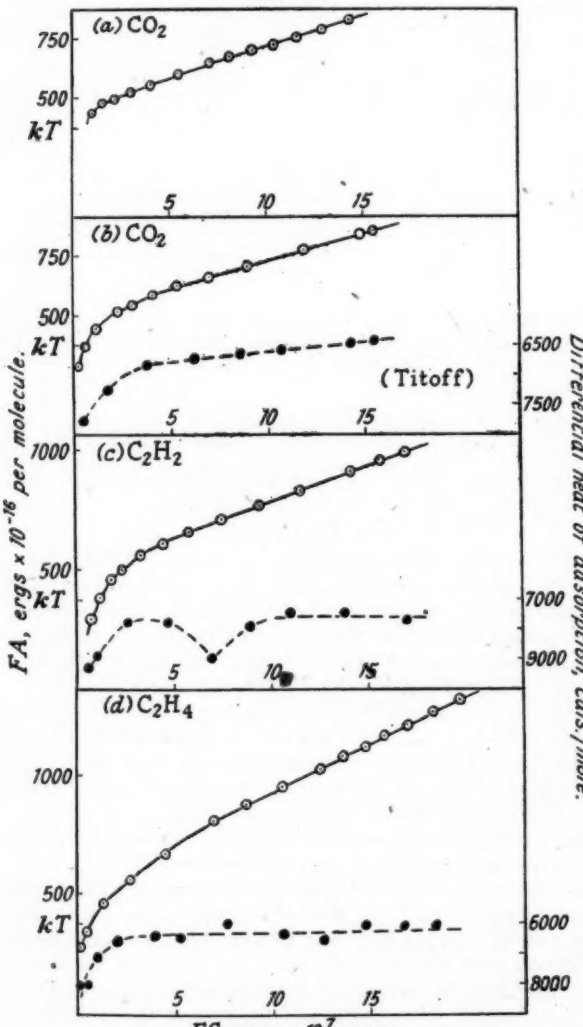
The rather sparse data for the differential heat of adsorption are consistent with the foregoing interpretation of the *FA–FS* curves. The heat of adsorption is made up of two parts: (*a*) heat of adsorption proper, due to the interaction of the adsorbed molecules with the adsorbent, and (*b*) the heat effect (a kind of two-dimensional Joule–Thomson effect) arising from the forces of attraction and repulsion between the adsorbed molecules themselves. Let the former be $\Delta H'$ cals./mole and the latter ΔJ; the measured differential heat of adsorption is then given by $\Delta H = \Delta H' + \Delta J$. Now, for those parts of the *FA –F* curve of constant slope, the orientation of the adsorbed molecules is constant, and since A is not far from A_0, the average separation of the adsorbed molecules in the layer does not alter much; ΔJ should therefore be nearly independent of x and of F. Also, for a surface of uniform activity $\Delta H'$ does not depend on the amount adsorbed either, so that ΔH should be independent of x and of F. Perhaps when the adsorbed layer is nearly full, ΔJ and therefore ΔH might increase slightly, due to the liberation of a heat of two-dimensional compression when the adsorbed molecules are pushed very close together. Where the *FA–FS* curve is non-linear, the orientation of the molecules, and hence their mutual interaction, varies with x, so that ΔJ is now a function of x and therefore of F: ΔH should now vary with F.

In Figs. 3 and 4, the curve of ΔH (measured calorimetrically) against FS is plotted alongside that of FA against FS, in those cases where sufficient data are available. It will be seen that the value of ΔH is fairly constant for the L_2 state, where the *FA–FS* curve is straight, and varies with FS for the L_1 state where the *FA–FS* curve is bent.

For a two-dimensional perfect gas, the interaction between the adsorbed molecules is zero, so ΔH should be independent of x or of F: in agreement with this, Magnus and Giebenhain have found that the differential heat of adsorption of carbon dioxide on silica gel is constant within narrow experimental limits throughout the Henry's law region (*Z. physikal. Chem.*, 1929, *A*, **143**, 265).

Calculation of the Specific Surface S *and of the Monolayer Capacity,* x_0.—Since the L_2 branch of the *FA–FS* curve is linear, its slope should, by analogy with films on water, be equal to A_0/S. Consequently, if a value can be assigned to A_0, the specific surface S can be calculated; A_0 is the incompressible area occupied on the adsorbent surface by the adsorbed molecules *when oriented in the manner proper to the* L_2 *state*, and exact assessment of it is difficult, for we do not know enough about either the orientation or the size and shape of molecules. Nevertheless, for small, nearly spherical molecules A_0 should not differ very greatly from the collisional area obtained from kinetic properties such as viscosity, or from the area calculated from the density of the bulk liquid, spherical or cubic molecules being assumed. An uncertainty of perhaps some 50% in A_0 and therefore in S is to be expected. A similar limitation on the accuracy of S necessarily attaches to all methods based on an estimate of the area occupied by the adsorbed molecules (*e.g.*, Harkins and Gans, *J. Amer. Chem. Soc.*, 1931, **53**, 2804; Paneth and Radu, *Ber.*, 1924, **57**, 1221; Brunauer and Emmett, *J. Amer. Chem. Soc.*, 1937, **59**, 1553; Brunauer, Emmett, and Teller, *ibid.*, 1938, **60**, 315).

FIG. 3.



References: (*a*), (*c*), (*d*)—Ref. (10), Table; (*b*)—Ref. (9), Table.

Adsorption on charcoal at 0°. Systems corresponding to type (iii) or (iv) of Fig. 1.

Full lines represent *FA* against *FS*; broken lines ΔH against *FS*.

As an example we calculate the specific surface for Charcoal I from the curve for its adsorption of carbon dioxide given in Fig. **3***a*. The slope B of the right-hand, straight portion is $2{\cdot}46 \times 10^{-22}$ molecules^{-1} g. The collision diameter of carbon dioxide from viscosity measurements is 4·6 A. (see Kennard, "Kinetic Theory of Gases," 1938), giving collisional area = 15·8 A.^{2}. Hexagonal packing being assumed, this would occupy *ca.* $15{\cdot}8 \times 1{\cdot}10 = 17{\cdot}8$ A.^{2} on the adsorbent surface if the molecule were spherical; actually, it is elongated and in the L_2 state would, by analogy with films on water, probably be oriented with its longest axis nearly or quite vertical. This would reduce the value of A_0 to, say, 15 A.^{2}, which, combined with the value of B, gives $S = 610$ sq. m. Titoff's charcoal (Fig. 3*b*) gives 580 sq. m. These are of the same order as, but rather larger than, the figures obtained by Paneth and Radu using dye adsorption from solution: animal charcoal 119—452 sq. m., and limewood charcoal 61—268 sq. m. (*Ber.*, 1924, **57**, 1215); the discrepancy is not surprising, for, apart from probable differences in the charcoals, the dye molecules, being large, would not be able to penetrate to some portions of the surface which would be open to carbon dioxide. Bangham, combining expansion results with adsorption-isotherm data and assuming that the films on charcoal obeyed the same equation of state as on mercury, obtained twelve values clustering around 176 sq. m. for a pinewood charcoal (*Proc. Roy. Soc.*, 1934, *A*, **147**, 180).

Rough estimates of the specific surface can also be based on the approximate slope of the L_1 branch of the *FA–FS* curve. Since the curve is no longer linear, the result cannot be accurate, but a useful approximation to S can frequently be obtained. The slope of the G branch at high pressure can be used similarly.

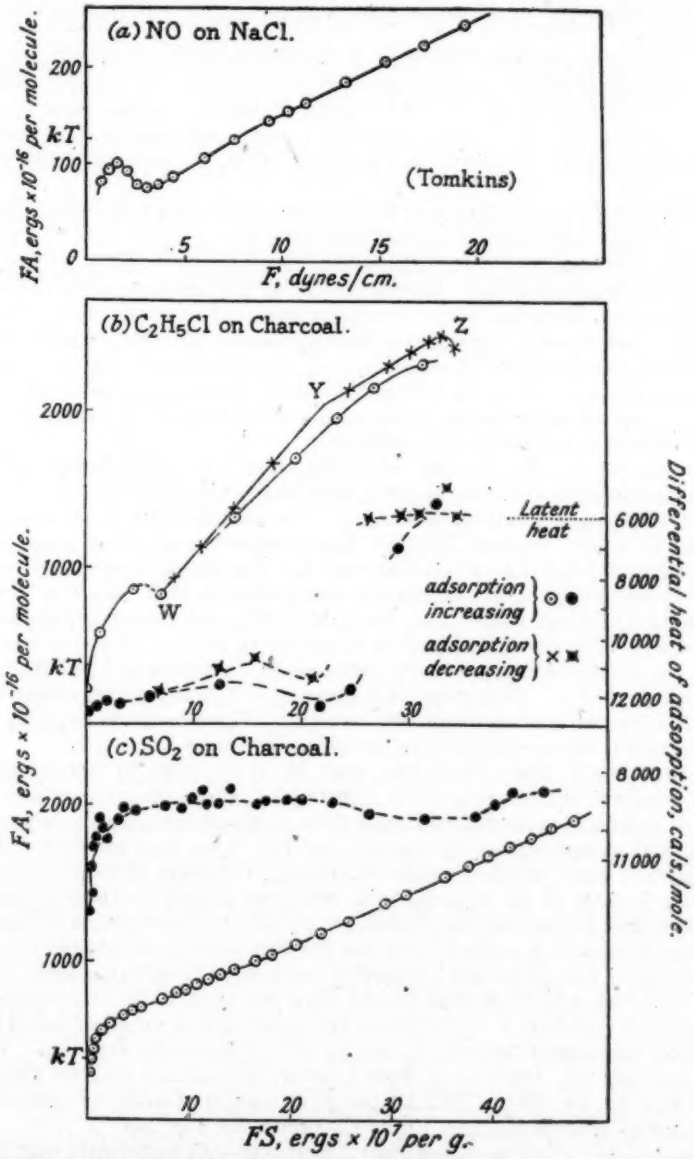
The correctness of the foregoing interpretation of the slope B can be tested by reference to a number of adsorbents of known specific surface, the value of S calculated by the relation A_0/S being compared with the directly measured value.

(a) *Nitric oxide on powdered sodium chloride* (Tomkins, *Trans. Faraday Soc.*, 1936, **52**, 643). The *FA–F* curve is shown in Fig. 4*a*, the values of F having been calculated from *FS* by using the measured value of S; the *FA–FS* curve required for our present purpose is, of course, of exactly the same shape. The extreme right-hand, linear branch corresponds to the L_2 state and its slope is $B = 2{\cdot}36 \times 10^{-20}$ molecules^{-1}. The collisional area of nitric oxide is 11·0 A.^{2} (Jeans, "Introduction to the Kinetic Theory of Gases," 1940, p. 183), and by arguments similar to those just used for carbon dioxide, remembering that the nitric oxide molecule is not quite

so elongated, we take the value of A_0 as *ca.* 11 A. Insertion of this in $S = A_0/B$ gives $S = ca.\ 4{\cdot}7 \times 10^4$ sq. cm., in good agreement with Tomkins's measured value of $4{\cdot}6 \times 10^4$ sq. cm.

(b) *Benzene vapour on mica* (Bangham and Mosallam, *loc. cit.*). The *FA–FS* curve is of the (iii)/(iv) type of Fig. 1 (with a bend downwards at the right-hand end due to multilayer formation, see later). The slope of the L_2 branch is $9{\cdot}1 \times 10^{-20} \pm 1{\cdot}1 \times 10^{-20}$ molecules^{-1}, the considerable uncertainty being due to hysteresis effects which make the exact location of the *FA–FS* curve uncertain. The most reasonable value to take for

FIG. 4.



References: (*a*)—Ref. (1), Table; (*b*), (*c*)—Ref. (13), Table.
Systems corresponding to types (iii) and (iv) of Fig. 1. In (*b*), layer thickening occurs.
Full lines represent *FA* against *FS*; broken lines *H* against *FS*.

A_0 in the L_2 state is that corresponding to the orientation of the molecules on edge, and this from *X*-ray data is 21·5 A.^{2} (Cox, *Proc. Roy. Soc.*, **1932**, *A*, **135**, 491). Combined with the value of *B*, this gives $S = 23{,}500 \pm 3000$ sq. cm., in satisfactory agreement with the measured value of 19,000 sq. cm.

(c) *Acetone on mica at* 19° (Bawn, *J. Amer. Chem. Soc.*, **1932**, **54**, 77). The average slope of the *FA–FS* curve over nearly the whole range, $FS = 0{\cdot}0073 \times 10^7$ to $0{\cdot}0316 \times 10^7$ erg, is $B = 3{\cdot}64 \times 10^{-19}$ molecules^{-1}; since the *FA–FS* curve is not straight (Fig. 2*h*) and the zero extrapolation of the isotherm is rather uncertain, this value of *B* is open to considerable error. Taking A_0 as equal to the area calculated from the density of the

bulk liquid, cubic molecules being assumed (since the molecules are not highly oriented in the L_1 state), *viz.*, 24·5 A.², we have $S = 6750$ sq. cm. Bawn's measured value is 6239 sq. cm. but such close agreement is fortuitous in view of the doubt as to the appropriate value of A_0, and the inexactitude inseparable from estimates based on non-linear *FA–FS* curves.

An indirect but very useful measure of the specific surface is the monolayer capacity, x_0, of the adsorbent, *i.e.*, the number of molecules which can be adsorbed in a completed monolayer; x_0 can be calculated from the slope B without any assumptions as to the value of A_0, for $x_0A_0 = S$, so $x_0 = S/A_0 = 1/B$. If the monolayer capacity is required in " practical " units such as c.c. (at N.T.P.) rather than in molecules, it is only necessary to express x in those units when drawing the curve of x against $\log p$; $1/B$ then gives the monolayer capacity in the desired units directly.

An estimate of the monolayer capacity, like that of the specific surface, can be accurate only if based on a linear branch—more particularly the L_2 branch—of an *FA–FS* curve. If based on an L_1, or a non-linear G branch, it is only a rough approximation. The I branch is, of course, useless for the purpose. The table on p. 701 gives the monolayer capacities for the L_2 state for a number of adsorbents and various adsorbates. In many cases the zero extrapolations of the semi-log isotherm curve are uncertain, but this should not greatly affect the values of B.

The monolayer capacity for a given adsorbent will necessarily depend both on the nature of the adsorbate and on its adsorbed state, since each of these factors will affect the value of A_0. The values of the monolayer capacity for the charcoals quoted are all of the same order, but for a given charcoal they depend on the nature of the gas; x_0 for a given charcoal should vary inversely as the incompressible area A_0 of the particular adsorbate in the L_2 orientation, if the same total area were equally accessible to all adsorbates no matter what their molecular size. This relationship between x_0 and A_0 cannot be tested rigorously, however, for equal accessibility is unlikely and the difficulty of estimating A_0 accurately still remains; but the gases adsorbed on charcoal I would not differ by more than two-fold in their incompressible areas, and the corresponding values of the monolayer capacity agree within these limits, and for gases of similar molecular structure they diminish as the number of atoms per molecule increases.

The monolayer capacity for a given gas and adsorbent should be nearly independent of temperature; if anything, A_0 might be expected to decrease slightly with rising temperature (by analogy with the van der Waals b for bulk fluids), implying a small *increase* in x_0. The values of the monolayer capacity from Titoff's data for carbon dioxide at − 76°, 0°, and 30° (see Table) show the expected approximate equality, as do Gregg's for sulphur dioxide at 0° and 40·3° on Charcoal I. The small temperature variation in monolayer capacity for ethyl chloride on Polanyi and Goldmann's charcoal at − 15·3° and 0° is in the correct sense.

According to Langmuir (*J. Amer. Chem. Soc.*, 1918, **40**, 1361), the monolayer capacity is the constant k_1 of the equation $x = k_1k_2p/(1 + k_2p)$. This equation gives rise to an *FA–FS* curve which, though resembling the " hydrogen type," has a slope which gradually increases as *FS* increases but becomes nearly constant, at $B = ca.\ 1{\cdot}2k_1$, for large values of x. This value of B gives $x_0 = 1/1{\cdot}2k_1$, which agrees tolerably well with k_1, considering that the *FA–FS* curve is never absolutely straight. The monolayer capacity is no longer calculable from the Langmuir equation if changes of state occur within the range considered.

Brunauer and his co-workers (*J. Amer. Chem. Soc.*, 1940, **62**, 1723; 1938, **60**, 309) have proposed a generalised form of the Langmuir equation for determining a quantity v_m, the monolayer capacity in c.c. (at N.T.P.). Their theoretical basis is, however, quite different from that of the present paper; in particular the isotherm is regarded as *continuous*, and is represented by a single equation from zero adsorption up to many molecular thicknesses of the adsorption layer, so the possible occurrence of changes of state in the adsorbed layer is not considered. Unfortunately, most of the experimental isotherms quoted by these workers in support of their views have too few experimental points at low pressures to permit the construction of the corresponding *FA–FS* graphs, and the replotting necessary in order to compare the two methods is deferred to a later communication. Meanwhile, it may be recalled that Brunauer's equation reduces to Langmuir's form at low pressures, so the value of v_m calculated with this simplified form should show the same order of agreement with x_0 as does k_1. If, however, a change of state occurs in the film within the experimental range to which the equation (whether full or reduced) is applied, agreement between v_m and x_0 can no longer be expected: for instance, the value obtained by Brunauer *et al.* (*loc. cit.*, 1940) for v_m from Lambert and Clark's data for the adsorption of benzene on ferric oxide gel is 0·081 g./g., *i.e.*, 23 c.c. (N.T.P.) per g., as compared with our value of 69 c.c. (N.T.P.), and this is a case where a change of state ($L_1 \rightleftharpoons I \rightleftharpoons L_2$) occurs (cf. Fig. 5*a*).

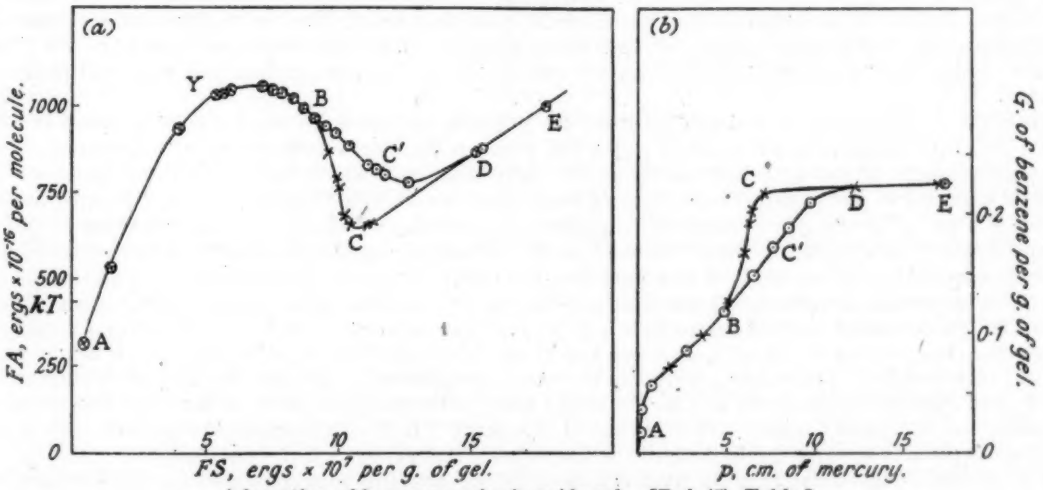
Formation of Multimolecular Layers on Non-porous Adsorbents.—At sufficiently high pressures, the film of a vapour adsorbed on a non-porous solid becomes more than one molecule thick: it passes over into a multilayer. This has been shown by a number of workers who have measured the adsorption of vapours on non-porous adsorbents having a known surface area so that the thickness of the layer could be calculated. The formation of adsorbed layers in excess of unimolecular is often assumed to occur in porous adsorbents also, but direct evidence is lacking. By constructing *FA–FS* graphs from the experimental data for non-porous adsorbents (see above) and examining their characteristics in the region corresponding to the transition from monolayer to multilayer, we can obtain criteria for the detection of multilayer formation in general, which should then be applicable to porous adsorbents. Such graphs have been constructed from the data of the following experiments: the lower fatty acids on mercury (Bosworth, *Trans. Faraday Soc.*, 1932, **28**, 903); benzene on mica (Bangham and Mosallam, *loc. cit.*); and acetone and benzene on vitreous silica (Palmer, *loc. cit.*). In every case

the graph shows a sudden change in slope at or near the point where $A = A_0$, corresponding to a completed monolayer. For example, with the vapours of valeric, propionic, and butyric acids on mercury, the *FA–FS* curve, which is very similar to the curve *ABCDE* of Fig. 5*a* for $A >$ *ca.* 20 A.², turns very sharply towards the *FS* axis when $A =$ *ca.* 20 A.², and continues to fall steeply, though (as far as can be judged from the small number of experimental points) not quite vertically, till, when the saturated vapour pressure is reached in the free space, the adsorbed layer is several molecules thick.

The *FA–FS* curve for benzene vapour on mica likewise shows a sudden turn towards the *FS* axis when *A* lies between 19 and 23 A.², where the monolayer must be just about complete (A_0 for benzene molecules oriented on edge is probably 21·5 A.², see above). The change in curvature, although not so sudden as in the mercury curves, was still sharp enough to produce a maximum in the *FA–FS* curve at a point corresponding to $A =$ 20—22 A.². The shape of the curve is very similar to the part *ABC* of Fig. 5*a*, though the significance of the branch *BC* is different in the two cases, for in Fig. 5*a* it corresponds to the I state whereas in the present case it denotes multilayer formation.

Bangham and Mosallam found that the inception of the second layer of molecules was accompanied by a sudden fall in the differential heat of adsorption calculated from the Clausius–Clapeyron equation. They say (*loc. cit.*, p. 560) " the adsorption energy is very nearly constant, its value, where the area per molecule exceeds 35 A.² being about 12,000 cals. per mole. As the area per molecule decreases from 35 to 25 A.² the energy falls to a minimum value " (about 7500 cals. per mole); " thereafter there is a slight rise to a value very near the normal heat of liquefaction." They regard it " as established that both the adsorption energy and the

FIG. 5.



Adsorption of benzene on ferric oxide gel. [Ref. (5), Table.]

slope of the isotherm undergo an abrupt change at *about* the adsorption value to be expected for a unimolecular film of molecules oriented on edge " (*loc. cit.*, p. 562).

Palmer noted that his data for benzene vapour on vitreous silica also lead to a maximum in the *FA–FS* curve; the shape of the curve is again very similar to *ABC* of Fig. 5*a*. It terminates when $p = p_s$ at a point corresponding to *C* on this figure, and the area per molecule is then 6·8 A.², corresponding to a layer about 3 molecules thick. The marked change in curvature (corresponding to point *Y* in Fig. 5*a*) occurs when *A* lies somewhere between 22 and 25 A.², *i.e.*, about the correct value for a completed monolayer. The curve from Palmer's data for acetone shows a sudden change in slope (not great enough to produce a maximum in the vicinity) at an *FS* value corresponding to some 22 A.², which again cannot be far from the value for a completed monolayer (*e.g.*, A_0 for acetone from bulk liquid density is 24·5 A.²). This curve is particularly interesting in that it shows a further sudden reduction in slope when $A =$ *ca.* 12 A.², corresponding to approximately two complete layers. Whether the completion of the second layer produces this effect in all systems cannot be decided owing to lack of experimental data.

On the basis of the foregoing results one may suggest that the formation of an adsorbed layer exceeding one molecule in thickness is signalised by a falling off in the *FA–FS* curve, commencing at some point *Y*, say; the downward bend may be great enough to produce a maximum in the neighbourhood of *Y*, but there is probably no discontinuity in the curve at *Y*. Since the thickening process presumably commences when the first layer is nearly or quite full, the amount adsorbed at *Y* should be near or equal to the monolayer capacity x_0 calculated from the slope of the part of the curve immediately preceding *Y*, if this is near enough to linear. The shape of the curve in the region corresponding to multilayer formation is very similar to that of the I region of a monolayer curve [cf. (iii) and (iv) of Fig. 1, also Fig. 5*a*]. Various means of distinguishing these are available, however, even if *S* is unknown; thus, if the transition $L_1 \rightarrow L_2$ or $G \rightarrow L_2$ has already occurred at *lower* pressures, the falling off cannot be due to the I state but must denote multilayer formation; but if the downward bend

commencing at *Y* is followed at *higher* pressures by the typical rising branch of the L_2 state, as in Fig. 5*a*, the bend must be ascribed to the I state and not to multilayer formation. Further, it seems likely on *a priori* grounds that the sudden fall in the differential heat of adsorption to a value near the latent heat of condensation, noted by Bangham and Mosallam, is a general effect associated with the inception of the second layer (Brunauer *et al.* make essentially this assumption in a simplified treatment of their general theory; *loc. cit.*, 1938); the transition from the L_1 or the G to the I state, on the other hand, would probably give rise to a much smaller, or even a negligible, change in the differential heat of adsorption.

Thickness of the Adsorbed Layer on Porous Adsorbents: the Theory of Capillary Condensation.—This well-known theory was first put forward by Zsigmondy (*Z. anorg. Chem.*, 1911, **71**, 356) in connection with the characteristic hysteresis loops obtained by van Bemmelen (*ibid.*, 1897, **13**, 233; 1898, **18**, 98) in the adsorption isotherm of water vapour on silica gel. Anderson (*Z. physikal. Chem.*, 1914, **88**, 212) also explained the hysteresis loops he obtained with benzene and alcohol vapour on silica gel, and Bachmann his loops with silica and ferric oxide gels (*Z. anorg. Chem.*, 1917, **100**, 41), in terms of capillary condensation. More recently, hysteresis loops have been studied experimentally by Lambert and Clark and Lambert and Foster (*loc cit.*). The isotherm for benzene on ferric oxide gel at 40° (*idem, loc. cit.*, 1932) is given in Fig. 5*b*. According to the capillary-condensation theory, branch *OAB* of this isotherm corresponds to an adsorbed layer, at most a few molecules thick, on the walls of the capillaries (Zsigmondy, *loc. cit.*; cf. Foster, *Trans. Faraday Soc.*, 1932, **28**, 652); at *B* " capillary condensation," in which the adsorbate condenses to a bulk liquid in the pores, sets in and proceeds till the pores are full of liquid (branch *BC'D*). The radius of the pore which is being filled at any pressure p is given by the Kelvin equation (*Phil. Mag.*, 1871, **42**, 448). Branch *DCB*, which is traced out when p is progressively reduced from its value at *D*, corresponds to the gradual emptying of the pores of their liquid, till at *B* only the wall layer remains; that branch *DCB* does not coincide with the capillary-filling branch *BC'D* is ascribed to irreversible effects associated with the formation of the liquid meniscus (Foster, *loc. cit.*; Cohan, *J. Amer. Chem. Soc.*, 1938, **60**, 433), or with the advance of the meniscus along the pore wall (Zsigmondy, *loc. cit.*).

When the *FA–FS* curve is constructed from the isotherm, it proves to be of the form shown in Fig. 5*a*. This is obviously analogous to curve (iii) or (iv) of Fig. 1, and is therefore characteristic of a *monolayer*. Branch *DE* shows no signs of the turn downwards at the right-hand end, which, according to the author's views, would be expected if the adsorbed layer became more than one molecule thick; in fact, *DE* provides a clear example of a curve for the liquid-condensed (L_2) state of a monolayer. This is the more striking in that Lambert and Foster's measurements were continued till the saturated vapour pressure was nearly reached.

The values of the differential heat of adsorption, calculated by means of the Clausius–Clapeyron equation, support the view that the adsorbed layer does not become thicker than unimolecular: the x–log p curves for 40° and 50° run sensibly parallel from about a point half-way between *A* and *B* (where experimental points first become close enough to permit judgment) and along *BCD* and *BC'D* respectively till *D* is nearly reached. The heat of adsorption is therefore practically the same (about 9500 ± 300 cals./mole) both before and after point *B*, and does not suddenly fall to near the latent heat (7900 cals./mole) at *B*, as would be expected if layer thickening—as in capillary condensation—began at this point. It must be admitted, however, that, since the heat of adsorption is so close throughout to the latent heat, this evidence is not conclusive.

It is especially significant that the hysteresis loop of the isotherm corresponds to the intermediate region I of the *FA–FS* curve; the branches *OB* and *DE* corresponding to the L_1 and the L_2 state are reversible within experimental limits, but the path between them depends on whether adsorption is decreasing or increasing. [Very similar behaviour occurs with films on water, where the I state, but not the L_1 or the L_2 state, is prone to hysteresis (Adam, *op. cit.*, p. 56).] The hysteresis is thus connected with the two-dimensional change of state $L_1 \rightleftharpoons I \rightleftharpoons L_2$ occurring within the monolayer itself, and not with the transition from a monolayer or a multilayer to bulk matter, as required by the capillary-condensation theory.

FA–FS curves of exactly the same general form as Fig. 5*a* are obtained from Anderson's isotherms for water vapour on silica gel (*loc. cit.*), and from Lambert and Foster's for ethyl alcohol vapour on ferric oxide gel (*loc. cit.*; see Fig. 2*h*). These particular isotherms have been selected solely because they have sufficient measurements at low pressures to make integration possible; and the isotherms obtained by the same authors at different temperatures or with different vapours, and some obtained by other workers, are so similar in general characteristics to Fig. 5*a* that there is no reason to doubt that the corresponding *FA–FS* curves, if they could be drawn, would have the same form as Fig. 5*b*. Isotherms of the type illustrated in Fig. 5*b*, then, signify that adsorption is confined to a monolayer, the hysteresis loop arising, not from capillary condensation, but from a transformation of state within the monolayer.

According to some versions of the capillary-condensation theory (*e.g.*, Patrick and McGavack, *J. Amer. Chem. Soc.*, 1920, **42**, 946), hysteresis is not an inevitable feature of capillary condensation, but may be an adventitious effect due, *e.g.*, to traces of adsorbed air. It is useful therefore to examine the *FA–FS* curves obtained from experiments where, though hysteresis was absent, the measurements were carried through to the saturated vapour pressure so that capillary condensation might perhaps still be expected from the theory. Such experiments are those with benzene vapour on silica gel (Lambert and Clark, *loc. cit.*) and ethyl chloride on charcoal (Polanyi and Goldmann, *loc. cit.*). In the first, the zero extrapolation of the semi-log isotherm curve is somewhat uncertain; consequently there is doubt whether the *FA–FS* curve is of the (iii)/(iv) type of Fig. 1, with the I region recessive, or of the (v)/(vi) type (the transition $G \rightarrow L_2$, or $L_1 \rightarrow L_2$, having taken

place at some lower pressure), but there is no doubt as to the absence of any bend towards the *FS* axis at the right-hand end of the curve, so that thickening of the adsorbed layer beyond unimolecular seems clearly ruled out.

The second case, the *FA–FS* curve of which is shown in Fig. 2*j*, is definitely of the (iii)/(iv) type of Fig. 1, both at − 15·3° and at 0°. Again, there is no falling off at the right-hand end of the L_2 branch, so the layer never exceeds unimolecular thickness—a conclusion borne out by the fact that the minimum value quoted by Goldmann and Polanyi for the (calculated) differential heat of adsorption is still 2800 cals./mole in excess of the latent heat.

It should not be concluded from the foregoing discussion that adsorption in porous adsorbents is *invariably* confined to a unimolecular layer. Three instances will be given in which adsorption seems definitely to proceed beyond the unimolecular stage at high relative pressures.

(a) *Water vapour on silica gel* (Lambert and Foster, *loc. cit.*, 1931). During a number of experiments successively on the same sample of gel, the isotherm shifted slightly each time in the direction of increased pressure. Lambert and Foster's experiment (4) at 70° and (5) at 60° have closely spaced points at higher pressures but not at lower ones, whereas Expt. (1), at 60°, extends to low pressures but has points widely spaced at higher pressures. In order to calculate the *FA–FS* curves for Expts. (4) and (5) it has therefore been necessary to make the slightly incorrect assumptions that the semi-log isotherm curve of Expt. (5) follows the same course as that of Expt. (1), and that the semi-log curve of Expt. (4) at 10° higher is parallel to the curve for Expt. (1). (The incorrectness is due to the slight shift of the isotherm, caused by each run, already noted.) Expts. (4) and (5), both of which ceased at pressures somewhat below the saturated vapour pressure p_s, gave isotherms with hysteresis loops and yielded *FA–FS* curves very similar to Fig. 5*a*. In a later experiment, still on the same gel, the adsorption measurements were commenced at a pressure slightly below p_s and to the right of the hysteresis loop, and were continued up to $p = p_s$; at a certain point in this region (when $x = x'$, say) the isotherm turned sharply upwards, $\Delta x/\Delta p$ suddenly becoming much larger though not infinite. Owing to the absence of the rest of the isotherm, the *FA–FS* curve cannot be constructed, but it is clear that the sudden rise in the isotherm must correspond to a sharp fall (though not vertical) in the *FA–FS* curve. Thickening of the layer beyond unimolecular may be inferred. Confirmation is afforded by applying the criterion that x' should be near in value to the monolayer capacity calculated from the slope of the L_2 branch of the *FA–FS* curve. Exact agreement is not to be expected: in view of the displacements in the isotherm with their implied reduction in monolayer capacity by each experiment, x' should be smaller than the x_0 values obtained in earlier experiments, since it is derived from the last experiment. The following figures are in agreement with this:

Expt. (4) at 70°	x_0 from *FA–FS* curve = 310 ± 12 c.c.
Expt. (5) at 60°	x_0 from *FA–FS* curve = 290 ± 12 c.c.
compare last expt.	x' from rise in isotherm = 270 ± 12 c.c.

It is significant that, though layer thickening occurs in this system, the hysteresis loop is not associated with the thickening process, but still corresponds to the I state of the monolayer. Lambert and Foster point out, however, that the lack of coincidence of ascending and descending points *may* extend outside the hysteresis loop, and this would imply that the conversion of the monolayer into a thicker layer may be attended by some degree of hysteresis. Such hysteresis would not be surprising, for this conversion, like the monolayer transition $L_1 \rightarrow I \rightarrow L_2$, must be regarded as a transformation of state.

(b) *Ethyl chloride on sugar charcoal* (Gregg, to be published). Marked hysteresis effects, together with much drift (very slow reduction in pressure over long periods) without, however, any well-defined hysteresis loop, make it doubtful how far the isotherm corresponded to true equilibrium conditions. Two *FA–FS* curves are shown in Fig. 4*b*, corresponding severally to adsorption increasing (circles) and decreasing (crosses). As far as point *Y*, each is fairly definitely of the (iii)/(iv) type of Fig. 1, branch *WY* corresponding to the L_2 state. The turn towards the *FS* axis which occurs at *Y* on the " adsorption decreasing " curve (it is much less sharp on the reverse curve, most probably because of hysteresis) strongly suggests the inception of adsorption in excess of a unimolecular layer. This inference is confirmed by the large and sudden reduction in the value of the heat of adsorption which occurred at the same time (see Fig. 4*b*—solid circles and crossed circles), the heat of adsorption for the branch *YZ* being close to the latent heat. A similar result was obtained on several successive runs. This thermal behaviour is strikingly similar to that in the layer-thickening range of Bangham and Mosallam's experiment with mica (*loc. cit.*), leaving little doubt that an increase in layer thickness starts at *Y*.

The slope of the L_2 branch *WY* of the " adsorption decreasing " curve (which is probably closer to equilibrium conditions than the " increasing " curve) gives the monolayer capacity as 47 ± 2 c.c. (at N.T.P.). If the layer-thickening process commences only when the monolayer is full, this value of x_0 ought to be the same as the value of x—say x''—at which sudden reduction in the differential heat occurs. For the " adsorption decreasing " run x'' lay between 44·2 and 41·2 c.c. (N.P.T.), and although this is appreciably different from x_0, yet the difference is probably no greater than can be accounted for by difficulties due to hysteresis.

(c) *Water vapour on copper oxide* (Bray and Draper, *Proc. Nat. Acad. Sci.*, 1926, **12**, 297). The zero extrapolation of the semi-log isotherm curve is somewhat uncertain, but the *FA–FS* curve, which is similar in shape to *AYBC* of Fig. 5*a*, undoubtedly shows a maximum between points corresponding to $x = 25{\cdot}5$ and 43 mg./g. (experimental points are rather widely spaced here) and falls off fairly steeply as x increases up to 214 mg./g.

at $p = p_s$. The slope of the curve immediately before the commencement of the bend gives x_0 = approx. 38 mg./g., whence it seems clear that layer thickening occurs, giving a film some 5 or 6 molecules thick at the highest pressure reached.

Doubtless, there are many other instances besides these three of adsorption in excess of a monolayer, but the paucity of low-pressure measurements makes them difficult to discover from the extant data. At the same time, the phenomenon appears to be much less common than the capillary-condensation theory would suggest. Even when thicker layers are formed, it does not necessarily follow that the adsorbate condenses in the pores on interstices as an ordinary liquid possessing the characteristic properties, such as surface tension and density, of the liquid in bulk. Bangham and his co-workers (*Trans. Faraday Soc.*, **1937**, **33**, 1463; **1938**, **34**, 554) have given several reasons, experimental and theoretical, for supposing that the multilayer of a vapour adsorbed on charcoal or on mica differs considerably in surface tension from the bulk liquid; they found that several different organic vapours, even when supersaturated, frequently failed to condense on to a multilayer of the same adsorbate on mica. Consistent with this is Lambert and Foster's observation (*loc. cit.*, 1931) that at no time, in their experiments on silica gel, could water be seen to condense on to the gel even when the saturated vapour pressure was reached in the free space and liquid water could be distilled on to the mercury of the manometer.

If the possibility of condensation to an ordinary liquid is rejected, there are still two different possible mechanisms by which the adsorption process can proceed from the point where the monolayer is just complete: (i) the multilayer may build up over the whole of the adsorbing area S at the same time, so that the molecular thickness of the layer is everywhere the same, and is a function of the pressure p, or (ii) commencing with the finest pores, the whole of the cross-section of each pore of a given radius r may become full in one step as soon as p has reached a critical value characteristic of r. Mechanism (ii) would thus be similar to that envisaged by the capillary-condensation theory except that the material filling the pores would no longer be in its ordinary bulk liquid condition, and the relationship between p and r would not be given by the Kelvin equation. Although there is no direct evidence for deciding between these alternatives, yet the similarity already demonstrated between adsorption on porous adsorbents and on non-porous ones, where mechanism (ii) is necessarily excluded, argues in favour of alternative (i).

The author gratefully acknowledges his indebtedness to Dr. D. H. Bangham for numerous helpful discussions.

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149. *5-Amino-2-hydroxybenzenesulphonamide and Some Related Compounds.*

By R. TECWYN WILLIAMS.

The synthesis of *5-amino-2-hydroxybenzenesulphonamide* from *p*-aminophenol is described. Its preparation was necessary because it could be an oxidation product of metanilamide in the animal body. *5-Amino-2-hydroxybenzenesulphonanilide*, *3-amino-4-hydroxybenzenesulphonanilide*, and *4-amino-2-hydroxybenzenesulphonanilide* have also been prepared.

A COMPARATIVE study of the metabolism of the therapeutically inactive isomerides of sulphanilamide, *i.e.*, orthanilamide and metanilamide, has necessitated the synthesis of certain aminohydroxybenzenesulphonamides. During the biological oxidation of metanilamide, the formation of three such amides is possible, namely, 2-hydroxy-, 4-hydroxy-, and 6-hydroxy-5-aminobenzenesulphonamide. Experimental evidence (unpublished) indicates that the oxidation product in rabbits is either the 4-hydroxy- or the 6-hydroxy- but not the 2-hydroxy-derivative.

The present paper deals with the synthesis of 2-hydroxy- and 4-hydroxy-5-aminobenzenesulphonamides, both of which were required for comparison with biological material. The synthesis of the 2-hydroxy-derivative (*p*-aminophenol-*o*-sulphonamide) was straightforward and is similar to that of 4-amino-2-hydroxybenzenesulphonamide (Thorpe and Williams, *Biochem. J.*, **1941**, **35**, 61). 5-Amino-2-hydroxybenzenesulphonic acid was acetylated, and the *acetyl* derivative converted into *5-acetamido-2-acetoxybenzenesulphonyl chloride*. *5-Amino-2-hydroxybenzenesulphon-amide* and *-anilide*, m. p. 159°, were then obtained by the usual methods. Post (*Annalen*, 1880, **205**, 62) prepared a crystalline solid, m. p. 98°, claimed to be 5-amino-2-hydroxybenzenesulphonanilide by the action of aniline on a crude chloride obtained by the direct action of phosphorus pentachloride at 100° on 5-amino-2-hydroxybenzenesulphonic acid. It differs considerably in m. p. from the anilide prepared here, but since the latter was prepared by a direct synthesis there is little doubt as to its structure.

3-Amino-4-hydroxybenzenesulphonamide has been synthesised by Kermack, Spragg, and Tebrich (J., 1939, 608) by reduction of the corresponding nitro-compound with sodium hydrosulphite, but much improved yields can be obtained by the use of tin and hydrochloric acid. Attempts to prepare it by the method used for the 5-amino-2-hydroxy-derivative were unsuccessful, although the corresponding *anilide* was obtained as expected. Acetylation of 3-amino-4-hydroxybenzenesulphonic acid, followed by treatment with phosphorus pentachloride, gave *3-acetamido-4-acetoxybenzenesulphonyl chloride*. Treatment of this chloride with aqueous ammonia, followed by evaporation, then hydrolysis of the residue with 2N-hydrochloric acid, gave a solution

which, on neutralisation and evaporation to dryness, gave a syrupy residue which did not crystallise. This non-crystalline residue gave a red coloration when diazotised and coupled with alcoholic dimethyl-α-naphthylamine (Marshall's diazo-reaction; Marshall, Emerson, and Cutting, *J. Amer. Med. Assoc.*, 1937, **108**, 935). Authentic crystalline 3-amino-4-hydroxybenzenesulphonamide, prepared from the corresponding nitro-compound after diazotisation, does not give a red colour with this reagent.

A sample of 4-acetamido-2-acetoxybenzenesulphonyl chloride (Thorpe and Williams, *loc. cit.*) being available, 4-*amino*-2-*hydroxybenzenesulphonanilide* was prepared and is described.

Experimetal.

5-*Acetamido*-2-*acetoxybenzenesulphonyl Chloride*.—A solution of 5-amino-2-hydroxybenzenesulphonic acid (Bauer, *Ber.*, 1909, **42**, 2107) (7 g.) in pyridine (12 c.c.) was treated with acetic anhydride (10 c.c.) with cooling. The mixture was kept at room temperature and *pyridine* 5-*acetamido*-2-*acetoxybenzenesulphonate* soon separated in thick rhombic plates, m. p. 143—144°, which were not quite pure after repeated crystallisation from absolute alcohol (Found: C, 52·0; H, 4·5. $C_{15}H_{16}O_6N_2S$ requires C, 51·1; H, 4·6%). The dried pyridine salt was triturated with phosphorus pentachloride (9 g.), and the product poured into ice-water. The solid was crushed under water; after 12 hours it was collected and dried (yield, 6·9 g.). 5-*Acetamido*-2-*acetoxybenzenesulphonyl chloride* crystallised from toluene in thick plates, m. p. 148—149° (Found: C, 41·4; H, 3·6; Cl, 12·1; CH_3·CO, 28·7. $C_{10}H_{10}O_5NClS$ requires C, 41·2; H, 3·45; Cl, 12·15; CH_3·CO, 29·5%).

5-*Amino*-2-*hydroxybenzenesulphonamide*.—The foregoing chloride (4 g.) was added to 50% ammonia solution (5 c.c.). Next day the filtered solution was evaporated on the water-bath, and the residue dissolved in 2N-hydrochloric acid (10 c.c.). 5-*Acetamido*-2-*hydroxybenzenesulphonamide* (0·75 g.) was slowly deposited (long flat rods from water, m. p. 215°). It was very sparingly soluble in cold water and gave a stable purplish-blue colour with ferric chloride (Found: N, 11·3; CH_3·CO, 17·45. $C_8H_{10}O_4N_2S,H_2O$ requires N, 11·3; CH_3·CO, 17·3%).

The filtrate from the acetyl compound was concentrated to 10 c.c., made 3N with respect to hydrochloric acid, and refluxed for an hour. The solution was cooled, neutralised with solid sodium carbonate, and extracted with ether for 24 hours. 5-*Amino*-2-*hydroxybenzenesulphonamide* (1·2 g.), obtained on evaporation of the ether, darkened considerably during recrystallisation from water and was obtained in clear brown prismatic rods, m. p. 202° (decomp.) (Found: C, 38·35; H, 4·25; S, 17·45. $C_6H_8O_3N_2S$ requires C, 38·3; H, 4·3; S, 17·0%). It was sparingly soluble in cold water and gave, with ferric chloride, a purplish-blue colour which quickly turned to purple, purple-red, and finally orange-red. It reduced ammoniacal silver nitrate and gave an orange-red coloration with nitrous acid, followed by alcoholic dimethyl-α-naphthylamine.

5-*Amino*-2-*hydroxybenzenesulphonanilide*.—Treatment of the above chloride (1 mol.) with aniline (2 mols.) in ethyl acetate gave 5-*acetamido*-2-*acetoxybenzenesulphonanilide*, which formed rectangular plates, m. p. 150° (decomp.), from aqueous alcohol (yield, quantitative) (Found: N, 7·9; CH_3·CO, 23·1. $C_{16}H_{16}O_5N_2S$ requires N, 8·0; CH_3·CO, 24·7%). The acetyl compound was boiled with 2N-hydrochloric acid for 15 mins.; from the resulting solution, after neutralisation, ether extracted the *anilide* (yield, 50%), which crystallised from hot water in balls of needles, m. p. 159° (Found: C, 54·9; H, 4·6; S, 11·5. $C_{12}H_{12}O_3N_2S$ requires C, 54·55; H, 4·5; S, 12·1%). It gave in aqueous alcohol a brown colour with ferric chloride; it quickly reduced ammoniacal silver nitrate, and in Marshall's diazo-test it gave a purple colour (similar to that given by *p*-aminophenol) which quickly faded to yellow.

3-*Acetamido*-4-*acetoxybenzenesulphonyl Chloride*.—3-Amino-4-hydroxybenzenesulphonic acid (B.D.H.) (10 g.) was dissolved in pyridine (50 c.c.) with cooling, acetic anhydride (20 c.c.) gradually added, and the mixture kept at room temperature. After 2 hrs. the whole crystallised on scratching. The *pyridine* 3-*acetamido*-4-*acetoxybenzenesulphonate* * (13 g.), recrystallised from alcohol, had m. p. 162° (Found: C, 50·0; H, 4·8; N, 7·4. $2C_{15}H_{16}O_6N_2S,H_2O$ requires C, 49·9; H, 4·7; N, 7·8%). It was very soluble in water. The pyridine salt (10 g.) was stirred with phosphorus pentachloride (10 g.), the product poured into ice-water, and the *chloride* recrystallised from toluene; m. p. 143° (yield, 6·9 g.) (Found: C, 41·45; H, 3·3; Cl, 12·05. $C_{10}H_{9}O_5NClS$ requires C, 41·2; H, 3·45; Cl, 12·15%).

3-*Amino*-4-*hydroxybenzenesulphonanilide*.—The foregoing chloride (3 g.) was dissolved in ethyl acetate (100 c.c.), and aniline (1·8 c.c.) added. After an hour, the separated aniline hydrochloride was removed and washed with a little ethyl acetate. The filtrates after 2 hours deposited 3-*acetamido*-4-*acetoxybenzenesulphonanilide* (2 g.). This was washed with water and recrystallised from aqueous acetone. A further amount was obtained on evaporation of the ethyl acetate mother-liquor. It formed stellate crystals, m. p. 205° (Found: N, 8·4; CH_3·CO, 24·8. $C_{16}H_{16}O_5N_2S$ requires N, 8·0; CH_3·CO, 24·7%). The acetyl compound was boiled with 3N-hydrochloric acid until it dissolved (*ca.* 1 hr.). The solution was filtered, diluted with water, and neutralised with sodium carbonate; 3-*amino*-4-*hydroxybenzenesulphonanilide*, which separated in poor yield, was purified by precipitation (needles, m. p. 172°) from alcoholic or ethyl acetate solution with light petroleum (Found: C, 54·4; H, 4·65; S, 11·6. $C_{12}H_{12}O_3N_2S$ requires C, 54·55; H, 4·5; S, 12·1%). It reduced ammoniacal silver nitrate and gave with ferric chloride a purple-red coloration which quickly turned red and finally gave a brown precipitate. It gave a bright yellow colour on diazotisation, but did not couple to form a red dye with 1% alcoholic dimethyl-α-naphthylamine. This lack of coupling is typical of *o*-aminophenols, *e.g.*, *o*-aminophenol, 4-amino-3-hydroxy- and 3-amino-4-hydroxy-benzenesulphonamide (cf. Thorpe, Williams, and Shelswell, *Biochem. J.*, 1941, **35**, 52).

4-*Amino*-2-*hydroxybenzenesulphonanilide*.—4-Acetamido-2-acetoxybenzenesulphonyl chloride (1·3 g.) (Thorpe and Williams, *loc. cit.*) was converted into 4-*acetamido*-2-*acetoxybenzenesulphonanilide* in the usual manner (yield, 1·4 g.). This was recrystallised from aqueous alcohol and formed prisms, m. p. 213—214° (Found: N, 8·0; CH_3·CO, 24·9. $C_{16}H_{16}O_5N_2S$ requires N, 8·0; CH_3·CO, 24·7%). On boiling with 50% hydrochloric acid it gradually dissolved; the solution, on cooling, deposited needles, presumably of the hydrochloride of the anilide. The solution was diluted with water, and the crystals dissolved; on neutralisation with sodium carbonate, 4-*amino*-2-*hydroxybenzenesulphonanilide* crystallised. It was purified by solution in ethyl acetate and precipitation with light petroleum. It formed needles, m. p. 184°, and gave in aqueous alcohol a faint brownish-red colour with ferric chloride. It gave a red Marshall diazo-test, but did not reduce ammoniacal silver nitrate (Found: C, 54·4; H, 4·6; S, 12·0. $C_{12}H_{12}O_3N_2S$ requires C, 54·55; H, 4·5; S, 12·1%).

University of Birmingham. [*Received, June 6th*, 1942.]

* This salt was prepared by Miss Jean Shelswell (Thesis, University of Birmingham, Dec., 1940).

150. *Quinoxaline Cyanines. Part I.*

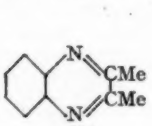
By A. H. Cook, J. Garner, and C. A. Perry.

2 : 3-Dimethylquinoxaline methiodide has been converted into a symmetrical carbocyanine and into unsymmetrical carbocyanines where the second auxochromic nucleus is benzoxazole, dimethylindole, quinoline, or *p*-dimethylaminobenzene. By using similar or modified methods to effect dye formation at a low temperature a series of dyes has been obtained derived from 1-phenyl-2-methylene- and 1-phenyl-2-methylene-3-methyl-dihydroquinoxaline.

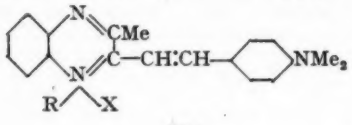
A strong bathochromic influence of the quinoxaline system is evident from the deep blue colour of the cyanines described.

The preparation of cyanine dyes from heterocyclic bases with reactive methyl groups or from their quaternary salts is well known. In addition to those derived from bases such as quinaldine and lepidine, cyanines derived from compounds containing other hetero-systems (oxazoles, thiazoles, imidazoles and quinazolines) have also been described. The only reference to the use of quinoxalines as the source of cyanines occurs in a recent patent (B.P. 506,720), though Kendall probably envisaged this possibility (*J. Soc. Dyers and Colourists*, 1936, **52**, 13) without specifically stating it. In the present paper it is shown that 2-methylquinoxalines possess the requisite activity for cyanine formation and a series of carbocyanines is described.

The starting point of these investigations was 2 : 3-dimethylquinoxaline (I). The methyl groups of this compound are known to be reactive, *e.g.*, towards benzaldehyde (Bennett and Willis, J., 1928, 1960), and were thus expected to form part of a cyanine chain. (I) yields only a monomethiodide (Bennett and Willis,



(I.)



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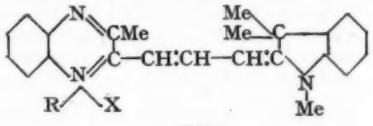


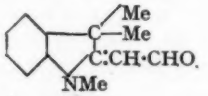
(III.)

loc. cit.), though in our experience this is formed only when anhydrous quinoxaline and not when the normal dihydrate is used. The monomethiodide readily formed cyanines, but before describing these it may be mentioned that no success attended attempts to extend the series by forming quaternary salts with ethyl or propyl iodide, benzyl chloride, *p*-nitrobenzyl chloride or 2 : 4-dinitrochlorobenzene even at the b. p. of the halides. Quaternisation of (I) and of other quinoxalines could nevertheless be achieved by heating with alkyl sulphonic esters, Grignard compounds, or particularly with alkyl sulphates.

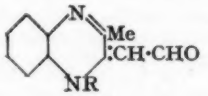
Quinoxalines not containing a methylene group in the 2-position failed to give colours by reactions similar to those described below, so there can be no doubt of the structure of the cyanines obtained.

(I) and methyl or ethyl sulphate react exothermally on gentle warming to give a low-melting, crystalline, water-soluble mono-metho- or -etho-sulphate accompanied by small amounts of green dyes. All of these quaternary salt preparations condensed to some extent with *p*-dimethylaminobenzaldehyde and other appropriate reactants, but as the resulting quinoxaline cyanines were usually unstable towards the hot reaction media, the usual cyanine preparative methods were inadmissible without modification; thus the preparation of these cyanines in quantity depended essentially on the discovery of conditions under which the condensations would proceed at room temperature. 2 : 3-Dimethylquinoxaline methiodide condensed only very slowly with *p*-dimethylaminobenzaldehyde in cold acetic anhydride, but in pyridine–acetic anhydride condensation was complete within 3—5 minutes with formation of the violet-blue dye (II; R = Me, X = acid radical). Similarly condensation of the methiodide with 1 : 3 : 3-trimethyl-2-methyleneindoline-ω-aldehyde (IV) afforded the violet-blue dye (III, R = Me) in remarkably high yield. These dyes could be obtained still more readily from the methosulphate without isolation of the intermediate salt. The *N*-ethyl analogues of (II) (R = Et) were likewise prepared, from crude ethosulphate.

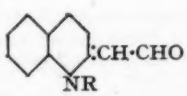
To extend this series it was necessary (*a*) to prepare a 2-ω-methylene-aldehyde (V) or a derivative of equivalent reactivity and then to condense this with a second quaternary salt or (*b*) to condense the quaternary



(IV.)



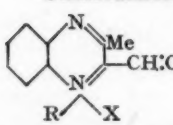
(V.)



(VI.)

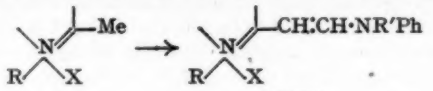
salts of 2 : 3-dimethylquinoxaline with a second aldehyde or equivalent derivative, *e.g.*, of the unknown aldehyde (VI) and others like it.

Unfortunately the methiodide of (I) and the methylene base obtained from it with alkali were so sensitive that attempts to prepare (V) by introducing the aldehydo-group with methylformanilide and phosphorus oxychloride (cf. Vilsmeier and Haack, *Ber.*, 1927, **60**, 119) were unsuccessful; for the same reason, equally unsuccessful were attempts to prepare the anilinovinyl compound (inset) from the quaternary salt and diphenylformamidine (cf. B.P. 344,409).



Turning to (*b*), we first attempted to prepare aldehydes analogous to type (VI) (cf. B.P. 486,780) which

are obtained by hydrolysing derivatives (VII, R′ = alkyl) with alkali. No difficulty was experienced in preparing compounds of type (VII) from methyldiphenylformamidine and quaternary salts of 2-methylbenz-

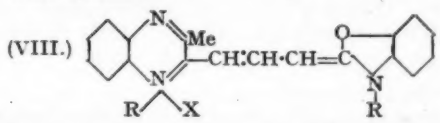


(VII.)

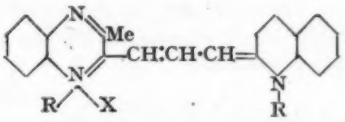
thiazole, 2-methylbenzoxazole or " Fischer's base," but, except for a small yield of 1-methyl-2-methylenebenzthiazolinealdehyde, no success attended attempts at hydrolysing the compounds.

It was interesting to find in this connexion that 1-phenyl-3-methyl-4-anilinomethylene-5-pyrazolone (Dains and Brown, *J. Amer. Chem. Soc.*, 1909, **31**, 1148) was not hydrolysed by alkali to the 4-aldehyde. On boiling for 3 hours with 4% aqueous-alcoholic hydrogen chloride it passed smoothly into bis-4 : 4′-1-phenyl-3-methyl-5-pyrazolonemethene. On the other hand 1-phenyl-3-methyl-4-methylanilinomethylene-5-pyrazolone was disrupted by boiling water into methylaniline and 1-phenyl-3-methyl-5-pyrazolone-4-aldehyde.

On attempting to condense compounds of type (VII, R = alkyl or H; the compounds where R = H are readily obtained from reactive quaternary salts and diphenylformamidine) with quinoxaline quaternary salts the instability of quinoxaline cyanines towards hot solvents was again encountered, so attempts in hot acetic anhydride failed. Eventually it became clear that transient appearance of the dyes was not conditioned by their instability towards acetic anhydride alone. They were stable towards boiling acetic anhydride or pyridine, but quickly disappeared in a mixture of the two. Under the normal preparative conditions in boiling acetic anhydride their instability was apparently due to mineral acid liberated during the reaction. So, on condensing quaternary salts of 2 : 3-dimethylquinoxaline with those of 2-anilinovinyl-benzoxazole or -quinoline derivatives in boiling acetic anhydride containing a large excess of sodium acetate the dyes (VIII) and (IX) were obtained.

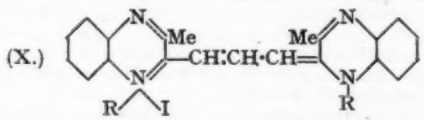


(VIII.)

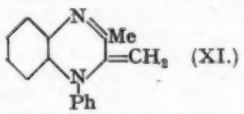


(IX.)

2 : 3-Dimethylquinoxaline methiodide failed to give significant yields of symmetrical dye on treatment with chloroform or chloral in caustic soda, ethyl orthoformate in acetic anhydride or pyridine, or with diphenylformamidine in hot acetic anhydride; all these methods gave coloured solutions, but in no case did they provide a practical route to the cyanine. Success was finally achieved by using sodium formate in acetic anhydride with strong cooling; 20—25% of the theoretical yield of (X, R = Me) was then obtained.



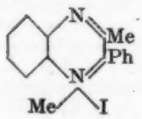
(X.)



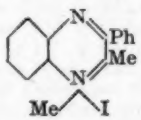
(XI.)

Analogues of the dyes already mentioned were obtained by first condensing *o*-aminodiphenylamine with diacetyl in alcoholic solution and precipitating the unstable methylene base (XI); in some instances no solvent was employed in preparing the quinoxaline and the crude product was used directly. (XI) and 1 : 3 : 3-trimethyl-2-methyleneindoline-ω-aldehyde yielded the analogue of (III) (R = Ph); in cold acetic anhydride moderate yields were obtained after 40 hours, but in acetic anhydride–pyridine excellent yields of crystalline dye were obtained after a few minutes. No condensation of (XI) with *p*-dimethylaminobenzaldehyde was observed in cold acetic anhydride even in presence of bases such as pyridine, piperidine, dimethylaniline or trimethylamine, or of acidic reagents. The condensation was, however, strongly catalysed by derivatives of boron such as the trifluoride or triacetate, particularly in presence of pyridine, but not by boric acid itself in presence of pyridine. The product was the analogue of (II) (R = Ph). Finally condensation of two molecular parts of (XI) with sodium formate in cold acetic anhydride containing acetyl chloride gave an excellent yield of the analogue of (X) (R = Ph).

Lastly homologues of some of the dyes already mentioned were examined. 3-Phenyl-2-methylquinoxaline readily gave a monomethiodide; in the crude state this gave blue colours with appropriate aldehydes, but on



(XII.)



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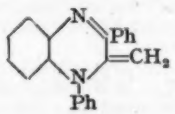
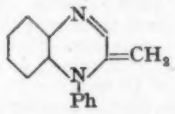


(XIV.)

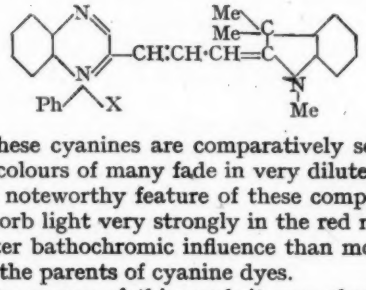


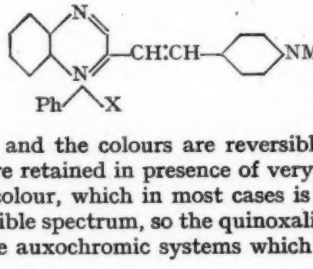
(XV.)

purification this property was lost; it thus follows that the main constituent of the crude methiodide is (XII) and that the useful component (XIII) arises in only negligible quantity. When phenylmethylglyoxal was condensed with *o*-aminodiphenylamine to give what, from its reaction, could only be the unstable methylene

base (XIV), the resulting carbocyanines were oily and clearly not homogeneous. They appeared to have a stability not greatly superior to that of these dyes already mentioned and were not further examined.

Quinoxalines derived from methylglyoxal and *o*-phenylenediamines may also give two structurally isomeric quaternary salts, only one of which would be of value in the present connexion. Therefore, on the basis of experience gained with phenylmethylglyoxal, only the reaction between methylglyoxal and *o*-aminodiphenylamine was examined. In cold acetic anhydride the unstable methylene base (XV) was evidently formed, but no colour developed in presence of either *p*-dimethylaminobenzaldehyde or 1 : 3 : 3-trimethyl-2-methyleneindoline-ω-aldehyde even when bases were added. In the case of the indoline aldehyde, however, the carbocyanine (XVI) was rapidly formed in presence of boron trifluoride but not of phosphorus halides. With *p*-dimethylaminobenzaldehyde, (XVII) was obtained in presence of phosphorus oxychloride but not boron trifluoride.

(XVI.) 

 (XVII.)

Most of these cyanines are comparatively soluble in water and the colours are reversibly discharged by alkali. The colours of many fade in very dilute solution but are retained in presence of very dilute acid.

The most noteworthy feature of these compounds is their colour, which in most cases is an intense blue. Solutions absorb light very strongly in the red region of the visible spectrum, so the quinoxaline system exerts a much greater bathochromic influence than most if not all the auxochromic systems which have previously been used as the parents of cyanine dyes.

During the course of this work it was observed that quinoxaline quaternary salts or methylene bases gave brilliant and unusually intense blue colours with *p*-nitrosodimethylaniline in mixtures of pyridine with acetic anhydride. These colours are almost certainly due to " aza-cyanines " (substituted anils). They are exceedingly unstable, however, and the colours faded to dull brown within 2—3 hours; their further examination was therefore abandoned.

Experimental.

2-(1 : 3-*Dimethylquinoxaline*)-1-(4-*dimethylaminobenzene*)*dimethincyanine* (II, R = Me).—(*a*) Dimethylquinoxaline methiodide (1 g.) was warmed gently with pyridine (4 c.c.), and the solution cooled and treated with *p*-dimethylaminobenzaldehyde (0·5 g.) in acetic anhydride (4 c.c.). The solution became immediately deep purple and then deep blue. The dye was deposited on the tube after 3—5 minutes and after 15 minutes was collected and washed with ether (yield, 1·25 g.). It was moderately soluble in water and crystallised from alcohol in minute needles, m. p. 244° (Found: N, 9·7. $C_{20}H_{22}N_3I$ requires N, 9·7%). Light absorption (alcohol): Diffuse band 5710—6170 A., max. 5950 A.

(*b*) Anhydrous 2 : 3-dimethylquinoxaline (1 g.) was warmed with slightly more than 1 mol. of methyl sulphate. As soon as reaction commenced the flask was cooled. Much heat was evolved and the product became greenish-blue and solidified. (The methosulphate is low-melting and readily soluble in water but may be purified by washing with benzene, in which it is insoluble.) To the dark product, acetic anhydride (4 c.c.) and *p*-dimethylaminobenzaldehyde (0·5 g.) in pyridine (4 c.c.) were added. The solution was gently warmed to initiate reaction and then kept. When cold the *methosulphate* of the dye was collected and washed with ether (yield, 60%). It crystallised from alcohol in needles, m. p. 182—183° (Found: N, 10·0. $C_{21}H_{25}O_4N_3S$ requires N, 10·1%).

2-(3-*Methyl*-1-*ethylquinoxaline*)-1-(4-*dimethylaminobenzene*)*dimethincyanine* (II, R = Et) was obtained in a similar manner by using ethyl sulphate in place of methyl sulphate in the preceding preparation. The *ethosulphate* of the dye separated from alcohol in needles with a green sheen, m. p. 170—171° (yield, 60% of the theoretical) (Found: N, 9·2. $C_{23}H_{29}O_4N_3S$ requires N, 9·4%).

2-(1 : 3-*Dimethylquinoxaline*)-2-(1 : 3 : 3-*trimethylindoline*)*trimethincyanine* (III, R = Me).—1 : 3 : 3-Trimethyl-2-methyleneindoline-ω-aldehyde (0·67 g.) was dissolved in pyridine and acetic anhydride (2 c.c. of each) and shaken with 2 : 3-dimethylquinoxaline methiodide (1 g.) at room temperature. After 30 minutes water (8 c.c.) was added, and the dye collected. The green residue (1·5 g., m. p. 188°) crystallised from alcohol (20 c.c.) in needles with a green lustre, m. p. 189—190° (0·9 g.) (Found: N, 8·3; I, 26·3. $C_{21}H_{26}N_3I$ requires N, 8·7; I, 26·3%). Light absorption (alcohol): Max., 6150 A. The iodide was soluble in alcohol, more difficultly in water, to give brilliant blue solutions. Solutions in ethyl acetate were mauve. The same dye was obtained in equally good yield by method (*b*) above, through the methosulphate. The methosulphate of the dye was soluble in the reaction medium and after addition of water was salted out with potassium iodide.

2-(1 : 3-*Dimethylquinoxaline*)-2-(1-*methylquinoline*)*trimethincyanine* (IX, R = Me).—Quinaldine methiodide (6 g.) and diphenylformamidine (4 g.) were intimately mixed and heated at 120° until the melt became very stiff. The cooled melt was triturated with dilute hydrochloric acid, and the insoluble yellow powder crystallised from alcohol. 2-*Anilinovinylquinoline methiodide* separated in yellow needles, m. p. 256° (decomp.) (Found: N, 7·3. $C_{16}H_{17}N_2I$ requires N, 7·2%) (cf. B.P. 344,409).

N-Methyldiphenylformamidine (21 g.), intimately mixed with 2-methylbenzoxazole ethiodide (28·9 g.), was heated at 170° for 5 minutes. The cold product was triturated with dilute hydrochloric acid, and the residual brick-red ethiodide crystallised from ethanol. 2-*Methylanilinovinylbenzoxazole ethiodide* had m. p. 212° and the yield, as in similar reactions (below), was almost quantitative (Found: N, 7·1. $C_{17}H_{17}ON_2I$ requires N, 7·1%). 2-*Methylanilinovinylbenzthiazole methiodide*, obtained in a similar manner, crystallised in needles, m. p. 244°, from acetic acid (Found: N, 6·7; I, 31·2. $C_{17}H_{17}N_2IS$ requires N, 6·8; I, 31·1%). 2-*Methylanilinovinylquinoline methiodide* was obtained similarly, except that more moderate heating (120° for 10 minutes) was sufficient. It separated from alcohol in needles, m. p. 271° (Found: I, 32·0. $C_{19}H_{19}N_2I$ requires I, 31·6%).

Of the preceding three anilinovinyl compounds, only the benzthiazole derivative was successfully hydrolysed to the aldehyde. The methiodide (25 g.) was boiled for 15 minutes with sodium hydroxide (50 g.) in water (120 c.c.). The solid residue was extracted with benzene, and the solvent removed. 1-*Methyl*-2-*methylenebenzthiazoline*-ω-*aldehyde* separated in needles (2 g.), m. p. 99°, from alcohol (Found: N, 7·3. $C_{10}H_9ONS$ requires N, 7·3%) (cf. B.P. 486,780).

2 : 3-Dimethylquinoxaline methiodide (2 g.) was boiled for 10 minutes with acetic anhydride (10 c.c.), 2-anilinovinyl-

quinoline methiodide (2 g.), and anhydrous sodium acetate (3 g.). The solution was diluted with water, and the dye salted out with sodium chloride. It separated from aqueous alcohol as a dark violet, crystalline powder (0·7 g.), m. p. >360° (Found: N, 11·6. $C_{23}H_{23}N_2Cl$ requires N, 11·8%). Light absorption (alcohol): Max. 5990, 5550 A.; I > II.

2-(1 : 3-*Dimethylquinoxaline*)-2-(1-*methylbenzoxazole*)*trimethincyanine* (VIII, R = Me).—2 : 3-Dimethylquinoxaline (2·9 g.) was quaternised with methyl sulphate (2 c.c.) as in previous examples, and the product added to a solution of 2-methylbenzoxazole methiodide (5 g.) and diphenylformamidine (3·6 g.) in acetic anhydride (20 c.c.) which had been previously boiled for 20 minutes. The whole was treated with anhydrous sodium acetate (7 g.) and boiled for 10 minutes. The solution was cooled and decomposed with water, and the dye salted out with potassium iodide. The *iodide* was crystallised repeatedly from dilute alcohol to give a dark greenish powder decomposing above 300° (Found: N, 8·9; I, 27·7. $C_{21}H_{20}ON_3I$ requires N, 9·2; I, 27·8%).

Bis-2-(1 : 3-*dimethylquinoxaline*)*trimethincyanine* (X, R = Me).—2 : 3-Dimethylquinoxaline methodide (2 g.) was stirred with acetic anhydride (20 c.c.), and sodium formate (1 g.) added with strong cooling in the early stages so that the temperature did not exceed 20—25°. After 30 hours the solution was diluted with water and aqueous potassium iodide, and the bronze-coloured dye (0·5 g.) crystallised from acetone to give needles with a bronze lustre, m. p. 204—205° (Found: N, 11·4. $C_{23}H_{23}N_4I$ requires N, 11·6%). The dye was only slightly soluble in alcohol or water and solutions were bright clear blue. Light absorption (alcohol): Max. 6880, 6300 A.; I > II. If the temperature was allowed to rise during the condensation, the yield of dye was usually negligible; occasionally, however, a very small amount of another blue dye, practically insoluble in boiling alcohol and crystallising in needles only from pyridine, was obtained.

2-(1-*Phenyl*-3-*methylquinoxaline*)-1-(4-*dimethylaminobenzene*)*dimethincyanine* (II, R = Ph).—*o*-Aminodiphenylamine (3 g.) was condensed with diacetyl (1·5 c.c.) without a solvent. The pasty product was diluted with acetic anhydride (8 c.c.), and 2 c.c. of a 20% solution of boron trifluoride in acetic acid added, followed by pyridine (10 c.c.) in which was dissolved *p*-dimethylaminobenzaldehyde (2·5 g.). The solution became brilliant blue at once but was kept for 24 hours and then diluted with water (50 c.c.). Sodium chloride was added; the oily deposit solidified when warmed with saturated brine. The *chloride* was obtained by repeated crystallisation from 95% alcohol as a microcrystalline powder which slowly decomposed at about 320° without melting (Found: N, 10·1; Cl, 8·8. $C_{35}H_{34}N_3Cl$ requires N, 10·4; Cl, 8·9%). It gave indigo-blue solutions in alcohol and water. Light absorption (alcohol): 6060—5720 A., max. 4890 A.

2-(1-*Phenyl*-3-*methylquinoxaline*)-2-(1 : 3 : 3-*trimethylindoline*)*trimethincyanine* (III, R = Ph).—*o*-Aminodiphenylamine (1 g.), dissolved in ether (10 c.c.), was condensed with diacetyl (0·5 c.c.); acetic anhydride (5 c.c.) was added, and ether removed under slight vacuum. 1 : 3 : 3-Trimethyl-2-methyleneindoline-ω-aldehyde (1·1 g.) was then added with pyridine (3 c.c.), and the whole kept overnight. Water (15 c.c.) was then added, and the green crystals, m. p. 152°, collected after 24 hours. This product (1·9 g.) was the *acetate*; it was very soluble in alcohol and crystallised from water in green needles, m. p. 154° (Found: N, 8·5. $C_{31}H_{31}O_2N_3$ requires N, 8·8%). Light absorption (alcohol): Max. 6530, 6080 A.; I > II.

Bis-2-(1-*phenyl*-3-*methylquinoxaline*)*trimethincyanine* (X, R = Ph).—*o*-Aminodiphenylamine (2 g.) was condensed with diacetyl (1 c.c.). Sodium formate (1 g.) and acetic anhydride (10 c.c.) were added, and the whole stirred at room temperature with cooling. No dye was formed until acetyl chloride (1 c.c.) was added; a bronze deposit then rapidly separated. After stirring overnight, water was added and the green crystalline *acetate* of the dye (2 g.) was collected and crystallised from water; m. p. 161° (Found: N, 10·1. $C_{35}H_{28}O_2N_4$ requires N, 10·4%). The colour is pure blue in water or alcohol, but the crude preparations are contaminated with a small amount of a green dye which is soluble not in water but in alcohol. When the acetic anhydride was diluted with aqueous sodium chloride, the *chloride* of the dye was salted out; it separated from water as a crystalline material with a bright brass-like lustre, decomposing above 300° (Found: N, 11·0. $C_{33}H_{27}N_4Cl$ requires N, 10·9%). Light absorption (alcohol): Max. 6990, 6410 A.; I > II.

2-(1-*Phenylquinoxaline*)-2-(1 : 3 : 3-*trimethylindoline*)*trimethincyanine* (XVI).—*o*-Aminodiphenylamine (1 g.) and methylglyoxal (0·7 g.) were condensed in acetic anhydride (5 c.c.). 1 : 3 : 3-Trimethyl-2-methyleneindoline-ω-aldehyde (1·1 g.) was added, followed by a 10% solution of boron trifluoride in acetic acid (1 c.c.) and then, with cooling, by pyridine (5 c.c.). After 10 minutes the solution was diluted with concentrated aqueous potassium iodide, and the oily deposit rubbed repeatedly with more aqueous potassium iodide and finally with ether. The *iodide* of the dye was finally crystallised repeatedly from alcohol to give a microcrystalline powder, m. p. 177° after softening at 150° (Found: N, 8·1; I, 23·1. $C_{28}H_{28}N_3I$ requires N, 7·9; I, 23·4%). Solutions of the dye in water are deep blue but in alcohol are violet. Light absorption (alcohol): Max., 6350, 5950, 5600 A.; I > II > III.

2-(1-*Phenylquinoxaline*)-1-(4-*dimethylaminobenzene*)*dimethincyanine* (XVII).—*o*-Aminodiphenylamine (1 g.) was treated with methylglyoxal (0·7 g.) in acetic anhydride (5 c.c.). The solution became slightly warm. When it was cold, *p*-dimethylaminobenzaldehyde (0·85 g.), followed by phosphorus oxychloride or acetyl chloride (2 c.c.), was added. With the first catalyst strong cooling is necessary to avoid violent reaction and acetyl chloride is therefore preferable. After 1 hour (using the former) or several hours (using acetyl chloride) the intensely green solution was diluted with aqueous potassium iodide. The resinous deposit was stirred several times with warm aqueous potassium iodide, and resin removed from the dried product by boiling with ether. The residue was crystallised repeatedly from alcohol to give the *iodide* of the dye as a microcrystalline solid with a green lustre, decomposing above 300°. The dye was practically insoluble even in warm water, but dissolved in alcohol or acetone to give dull green solutions (Found: N, 8·5. $C_{31}H_{22}N_3I$ requires N, 8·7%).

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151. *Vital Stains. Part I.*

By ALAN A. GOLDBERG.

Vital stains of the trypan-blue type are selectively deposited in tumour tissue when administered parenterally to tumour-bearing animals. A series of such stains has been synthesised bearing iodine or arsenic as a substituent part of the molecule in order to utilise the dye as a carrier of iodine or arsenic into the site of the tumour, where these elements may exert some therapeutic action.

THE intravital staining of malignant neoplasms as a therapeutic measure has been studied with a number of dyes in both animals and man, although in general the results have been negative as far as retardation of tumour growth is concerned (Weil, *J. Cancer Research*, 1916, **1**, 95; Marsh and Simpson, *ibid.*, 1928, **11**, 417; Engel, *Z. Krebsforsch.*, 1925, **22**, 365; Munck, *ibid.*, 1928, **26**, 377; Glasunow, *Z. Zellforsch.*, 1928, **6**, 773). This property of selective intravital deposition is possessed by trypan-blue to a high degree: after injection of the dye into a tumour-bearing animal the tumour stroma becomes heavily stained and there is a general deposition in the reticulo-endothelial cells (Ludford, *Proc. Roy. Soc.*, 1929, *B*, **104**, 493). Evans-blue—an analogue of trypan-blue—when administered intravenously to mice and rabbits bearing spontaneous or implanted tumours, produces general staining with very marked selective deposition of the dye in and about the neoplasms and their metastases; although the dye does not penetrate the cancer cells themselves, the necrotic areas become uniformly stained and there is an abundant segregation of the dye in the fibroblasts and macrophages of the stroma (Duran-Reynals, *Amer. J. Cancer*, 1939, **35**, 98). Similar observations on the intravital activity of isamine-blue and Evans-blue in tumour-bearing humans have been made respectively by Bernhardt (*Z. Krebsforsch.*, 1928, **27**, 221) and Brunschwig, Clark, and Schmitz (*Arch. Path.*, 1940, **30**, 902).

It was therefore of interest to examine the intravital activity of a series of dyes of the trypan-blue type bearing iodine or arsenic as a constituent part of the molecule; provided there was no impairment in the selective substantivity of the dye molecule, the latter would be used as a carrier of iodine or arsenic into the site of the tumour, where these elements may exert some therapeutic action.

The dyes synthesised were of the extended trypan-blue type containing iodine in the terminal and/or the central components; in the case of the arsenical dyes the terminal components alone were arsenated. In general an iodinated arylamine (terminal component) was diazotised and coupled with a heteronuclear aminonaphtholdisulphonic acid in mineral acid solution in the *o*-position to the amino-group; two molecules of this monoazo-dye were then coupled in alkaline solution with a tetrazotised diaryldiamine (central component) in the *o*-position to the hydroxyl groups.

5-Iodo-*o*-toluidine was a suitable terminal component; arylamines containing two iodine substituents, such as the di-iodotoluidines, were too sparingly soluble for the purpose, since even when dissolved in cold sulphuric acid and diazotised with nitrosylsulphonic acid it was not possible to attain the physical conditions necessary for coupling. Introduction of solubilising groups, however, overcame this difficulty, since 2 : 6-di-iodosulphanilic, 2 : 6-di-iodoarsanilic, and 4 : 6-di-iodoanthranilic acids diazotised and coupled smoothly in mineral acid solution with the aminonaphtholdisulphonic acid.

For the central component benzidine, *o*-tolidine, and dianisidine were employed, giving a series of vital stains of the extended trypan-blue type bearing iodine in the terminal components alone. In order to obtain dyes carrying iodine in the central component it was necessary to obtain iodinated derivatives of benzidine. The iodination of benzidine with iodine or iodine monochloride gave products which could not be obtained pure and were too sparingly soluble for the purpose in mind. Attempts to prepare a heteronuclear di-iodobenzidine of known orientation by reduction of *m*-iodonitrobenzene to the corresponding hydrazo-compound, followed by a benzidine transformation, were not successful. Benzidine-2 : 2′-disulphonic acid, however, was iodinated smoothly with iodine monochloride to yield a soluble di-iodobenzidinedisulphonic acid; this resisted further iodination and in consequence it seems probable that the iodine occupies the 5 : 5′-positions and that entrance of iodine into the 3 : 3′-positions is sterically prevented.

Iodination of 4 : 4′-diaminodiphenylmethane yielded a *di-iodo-* and a tetraiodo-derivative, presumably the 3 : 3′- and the 3 : 3′ : 5 : 5′-compound, respectively. The former is sufficiently soluble for tetrazotisation and coupling; dyes prepared from this central component, however, are not strictly of the trypan-blue type.

Physiological work carried out by Drs. Pick, Scholl, and Wiesner (to be published elsewhere) with some of these vital stains shows that the presence of iodine does not impair in any way the property of selective deposition in tumour tissue which appears to be characteristic of all dyes of the trypan-blue structure. Doses of 0·75 g./kg. per day of the iodinated vital stains A and B (pp. 715 and 716) may be administered subcutaneously to mice on 3 consecutive days without toxic symptoms arising. In addition to general staining (blue with A and red-purple with B) there is a rapid segregation of stain in the cells of the reticulo-endothelial system; the dye accumulates in the kidney cortex, liver, spleen and testes of normal mice, and with mice bearing implanted tumours of the Crocker and Ehrlich type there is marked localisation of the dye in those parts of the tumour where the tumour cells penetrate into the muscular and connective tissue of the host.

EXPERIMENTAL.

5-Iodo-o-toluidine Hydrochloride (compare Wheeler and Liddle, *Amer. Chem. J.*, 1909, **42**, 498).—Iodine (60 g.) and precipitated calcium carbonate (60 g.) were ground together and added to a mixture of *o*-toluidine (30 g.), ether (75 c.c.), and water (45 c.c.), which was then refluxed, with shaking at intervals, for 4 hrs. Next day water was added, the unchanged toluidine distilled in steam, and the residual calcium carbonate and 5-iodo-*o*-toluidine collected and extracted with boiling alcohol. On evaporation of the alcohol (charcoal) the iodotoluidine crystallised in purple needles (55 g.), which were dissolved in the minimal amount of dilute hydrochloric acid (1 : 6) and filtered to remove any di-iodotoluidine, the hydrochloride of which was almost insoluble. The filtrate (charcoal) was chilled, and hydrochloric acid (50 c.c.) added; the iodotoluidine hydrochloride then separated in almost white needles (42 g.), m. p. 214—216°.

Sodium 2-(5′-Iodo-o-tolueneazo)-1-amino-8-naphthol-3 : 6-disulphonate.—A fine suspension of 5-iodo-*o*-toluidine hydrochloride (26 g.) in water (380 c.c.) and 10N-hydrochloric acid (60 c.c.) was diazotised just below 0° with sodium nitrite (7·5 g. in the minimum amount of water); after 30 minutes' rapid stirring the diazonium chloride formed a thin brown suspension. An ice-cold solution of sodium hydrogen 1-amino-8-naphthol-3 : 6-disulphonate (36 g.) in water (150 c.c.)

and 5N-sodium hydroxide (20 c.c.) was added slowly, and stirring continued for 5 hrs. at 0—5°, any tendency to frothing being suppressed by the addition of a few drops of octyl alcohol. 5N-Sodium hydroxide (40 c.c.) was added, and the dark red liquid kept for 12 hrs. and then warmed at 40° for 1 hr. in order to complete the coupling. 5N-Sodium hydroxide (40 c.c.) was again added, the mixture chilled in ice–salt, and the dark precipitate removed, and dissolved in boiling water (210 c.c.) and the theoretical amount of sodium hydroxide, and reprecipitated in the cold with a small excess of dilute sulphuric acid as the sodium hydrogen salt; on drying at a low temperature the monoazo-dye was obtained as a maroon-black microcrystalline powder (25 g.). For analysis it was converted into the *disodium* salt and recrystallised four times (Found: I, 20·3. $C_{17}H_{12}O_7N_3IS_2Na_2$ requires I, 20·9%). The disodium salt is very soluble in water with production of a deep red solution.

Sodium 3 : 3′-*Dimethyldiphenyl*-4 : 4′-*bis*-[2″-*azo*-8″-*amino*-1″-*hydroxy*-3″ : 6″-*disulphonaphthalene*-7″-(5‴-*iodo*-*o*-*azotoluene*)] (A).—*o*-Tolidine (4·24 g.) was kept in water (120 c.c.) and 10N-hydrochloric acid (18 c.c.) for several hours to facilitate subsequent dissolution, then warmed with rapid stirring and quickly cooled below 0°; the fine suspension of the hydrochloride thus obtained was tetrazotised with a cold concentrated solution of sodium nitrite (2·4 g.). After 15 mins., the solution was added slowly to a rapidly stirred, ice-cold solution of the foregoing monoazo-dye (24 g.) in water (280 c.c.) and 5N-sodium hydroxide (100 c.c.). The mixture, which gradually became deep purple, was stirred at a low temperature for 6 hrs., kept overnight, warmed at 50° for 2 hrs., and chilled; the tetrakisazo-dye, precipitated by cold hydrochloric acid (60 c.c.), was collected, dried at a low temperature, and obtained as a blue-black powder (17 g.). For analysis it was precipitated from a cold solution in water (200 c.c.) and 5N-sodium hydroxide (10 c.c.) with dilute sulphuric acid and converted into the *tetrasodium* salt, which was dialysed and recrystallised four times (Found: I, 18·0; Na, 6·7. $C_{48}H_{34}O_{14}N_{10}I_2S_4Na_4$ requires I, 17·5, Na, 6·35%). The tetrasodium salt is very soluble in water, giving a fine purple solution.

The benzidine and dianisidine analogues of the above tetrakisazo-dye were similarly prepared.

2 : 6-*Di-iodoarsanilic Acid* (compare Bertheim, *Ber.*, 1910, **43**, 535).—Potassium iodide (35 g.) in water (100 c.c.) was added during 30 mins. to a warm solution of arsanilic acid (11 g.), potassium iodate (10 g.), and sulphuric acid (35 c.c.) in water (500 c.c.); the white precipitate formed slowly turned dark brown. The mixture was heated, with frequent shaking, on the water-bath for 3 hours and cooled, the dark residue extracted with warm dilute sodium hydroxide solution, and the insoluble tri-iodoaniline (5 g.) removed. Sodium sulphite (*ca.* 1 g.) was added to the filtrate and then an excess of hydrochloric acid; the di-iodoarsanilic acid was precipitated as a white flocculent mass (12 g.) (Found in material recrystallised from dilute alcohol: I, 54·3. Calc.: I, 54·1%).

Sodium 2-(2′ : 6′-*Di-iodo*-4′-*arsonobenzeneazo*)-1-*amino*-8-*naphthol*-3 : 6-*disulphonate*.—To a strongly cooled solution of di-iodoarsanilic acid (18·8 g.) in water (200 c.c.) and 5N-sodium hydroxide (10 c.c.), sodium nitrite (3·0 g., in a small amount of water) was added, followed dropwise, with stirring, by 10N-hydrochloric acid (25 c.c.). The heavy yellow precipitate formed redissolved with production of a thin yellow suspension of the diazonium salt. An ice-cold solution of sodium hydrogen 1-amino-8-naphthol-3 : 6-disulphonate (14·4 g.) in water (200 c.c.) and 5N-sodium hydroxide (25 c.c.) was added during 60 mins., the deep red liquid stirred at 0° for 10 hrs., kept overnight, heated at 40° for 1 hr., and chilled, and the bulk of the dye collected. The filtrate was neutralised with sodium carbonate, evaporated to smaller volume, and cooled, and a small excess of hydrochloric acid added; a further crop of the dye was then obtained. The combined precipitates were dissolved in boiling water (125 c.c.) and the smallest amount of sodium carbonate to effect solution and, after filtration, reprecipitated in the cold with a slight excess of dilute sulphuric acid; the dye, dried at a low temperature, was obtained as a dark maroon powder (15 g.). For analysis the monoazo-dye was converted into the *tetrasodium* salt, which was recrystallised several times (Found: I, 27·8. $C_{16}H_8O_{10}N_3I_2S_2AsNa_4$ requires I, 28·6%).

Sodium 3 : 3′-*Dimethyldiphenyl*-4 : 4′-*bis*-[2″-*azo*-8″-*amino*-1″-*hydroxy*-3″ : 6″-*disulphonaphthalene*-7″-(*azo*-2‴ : 6‴-*di-iodobenzene*-4‴-*arsonate*)].—*o*-Tolidine (4·2 g.) in water (75 c.c.) and hydrochloric acid (15 c.c.) was tetrazotised (sodium nitrite, 2·1 g.), and the solution added during 30 mins. to a stirred ice-cold solution of the foregoing monoazo-dye (25 g.) in water (130 c.c.) and 5N-sodium hydroxide (80 c.c.). After the usual procedure the dye was precipitated in the cold by hydrochloric acid (75 c.c.) as the sodium hydrogen salt, which was collected by centrifuging, drained (pump), and dissolved in boiling water and the minimum amount of sodium carbonate to form the octasodium salt. The dye was reprecipitated in the cold with a small excess of dilute sulphuric acid, collected, and reconverted into the *octasodium* salt, which was dialysed, recrystallised twice from the smallest amount of water, and obtained in dark maroon leaves (8 g.), which formed a deep brown-red solution in water (Found: I, 24·4; S, 6·8. $C_{44}H_{26}O_{20}N_{10}I_4S_4As_2Na_8$ requires I, 25·3; S, 6·4%).

3 : 3′-*Di-iodo*-4 : 4′-*diaminodiphenylmethane*.—Diaminodiphenylmethane (20 g.), iodine (50 g.), calcium carbonate (30 g.), water (50 c.c.), and ether (30 c.c.) were refluxed for 7 hrs., the viscous mass extracted with boiling alcohol (600 c.c.), the calcium carbonate removed, and the filtrate evaporated to small volume under reduced pressure. On addition of water a thick black tar was precipitated which became friable on standing. This was ground and warmed with water (500 c.c.) and hydrochloric acid (75 c.c.); the di-iodo-derivative dissolved, leaving a residue (4 g.) of more highly iodinated compounds. The filtered solution (charcoal) was basified with cold sodium carbonate, the precipitated base removed and suspended in water (250 c.c.), and sulphuric acid added (5 c.c.); the di-iododiaminodiphenylmethane sulphate separated as a light brown powder (the sulphate of diaminodiphenylmethane is soluble under these conditions). The sulphate (18 g.) was collected, washed, and suspended in cold water, and sodium carbonate added; 3 : 3′-*di-iodo*-4 : 4′-*diaminodiphenylmethane* was then obtained as a purple-black micro-crystalline powder (16 g.), m. p. 80—85° after recrystallisation from alcohol (Found: I, 56·4. $C_{13}H_{12}N_2I_2$ requires I, 56·5%).

Potassium 1-(4′-*Arsonobenzeneazo*)-2-*amino*-8-*naphthol*-3 : 6-*disulphonate*.—Arsanilic acid (10·9 g.) in water (100 c.c.) was diazotised with sodium nitrite (3·5 g.) and 10N-hydrochloric acid (25 c.c.), and an ice-cold solution of potassium hydrogen 2-amino-8-naphthol-3 : 6-disulphonate (18 g.) in water (100 c.c.) and 5N-potassium hydroxide (10 c.c.) added. After 8 hrs.' stirring, the scarlet liquor was kept overnight, warmed at 50° for 1 hr., and exactly neutralised, and the dye salted out with potassium chloride (20 g.). After standing on ice for 12 hours, the precipitate was collected and recrystallised from the minimum amount of boiling water, the *monoazo-dye* forming red-black leaves (13 g.), very soluble in water, giving an intense scarlet solution (Found in recrystallised salt: S, 9·6. $C_{16}H_{10}O_{10}N_3S_2AsK_4$ required S, 9·2%).

Potassium 3 : 3′-*Di-iododiphenylmethane*-4 : 4′-*bis*-(2″-*azo*-7″-*amino*-1″-*hydroxy*-3″ : 6″-*disulphonaphthalene*-8″-*azobenzene*-4‴-*arsonate*).—Di-iododiaminodiphenylmethane (4·5 g.) in water (100 c.c.) and 10N-hydrochloric acid (20 c.c.) was tetrazotised at 0° (sodium nitrite, 1·4 g.) and after 15 mins. the clear solution was added slowly to an ice-cold solution of the foregoing dye (12 g.) in water (130 c.c.) and 5N-potassium hydroxide (80 c.c.), the colour becoming blood-red. After 16 hrs.' stirring, the solution was warmed at 50° for 1 hr., and the dye isolated as its *octapotassium* salt, a dark microcrystalline powder (5 g.) very soluble in water (Found: I, 14·3; S, 7·3. $C_{45}H_{26}O_{20}N_{10}I_2S_4As_2K_8$ requires I, 13·6; S, 6·85%).

2 : 6-*Di-iodosulphanilic Acid* (compare D.R.-P. 129,808).—A solution of sodium sulphanilate (19·5 g.) in water (50 c.c.) at 60° was added during 30 minutes to a rapidly stirred solution of iodine monochloride (33 g.) and hydrochloric acid (37 c.c.) in water (250 c.c.) at 60°. After 3 hrs.' stirring at 70—80°, the liquid was kept overnight and filtered, the precipitate dissolved in boiling water (300 c.c.) and 5N-sodium hydroxide (25 c.c.), and a little sodium bisulphite added

(charcoal), followed by an excess of hydrochloric acid; the di-iodosulphanilic acid separated in heavy white needles (36 g.) (Found in recrystallised material: I, 59·5. Calc.: I, 59·7%).

5 : 5′-*Di-iodobenzidine*-2 : 2′-*disulphonic Acid*.—A solution of benzidine-2 : 2′-disulphonic acid (34·4 g.) in water (50 c.c.) and 5N-sodium hydroxide (30 c.c.) at 80° was added during 60 minutes to a solution of iodine monochloride (65 g.) in water (200 c.c.) and hydrochloric acid (100 c.c.) at 80°. After 4 hrs.' stirring, the dark liquid was kept overnight and chilled, and the precipitate collected; a further crop was obtained by evaporation of the filtrate to 100 c.c. and cooling. The combined precipitates were suspended in hot water (200 c.c.) and treated with sulphur dioxide to remove free iodine, and 5N-sodium hydroxide added until a clear solution at p_H 8·0 was obtained. This solution (charcoal) was evaporated until crystallisation on the water-bath began (120 c.c.), a saturated solution of sodium chloride (20 g.) added, and the orange crystalline precipitate (40 g.) collected after standing on ice for 16 hrs. Recrystallisation from the minimal amount of boiling water (120 c.c.) gave *sodium* 5 : 5′-*di-iodobenzidine*-2 : 2′-*disulphonate* in pale orange leaves (28 g.) (Found: I, 39·4. $C_{12}H_8O_6N_2I_2S_2Na_2$ requires I, 39·7%). From the mother-liquor a further quantity of almost pure substance (14 g.) was obtained. The salt was very soluble in water, giving a pale orange solution.

Sodium 2-(2′ : 6′-*Di-iodo*-4′-*sulphobenzeneazo*)-1-*amino*-8-*naphthol*-3 : 6-*disulphonate*.—To an ice-cold solution of 2 : 6-di-iodosulphanilic acid (42·8 g.) in water (240 c.c.) and 5N-sodium hydroxide (20 c.c.) was added a concentrated solution of sodium nitrite (7·2 g.), followed by 5N-hydrochloric acid (80 c.c.); the diazonium chloride formed a bright yellow suspension. After 30 mins.' stirring, an iced solution of sodium hydrogen 1-amino-8-naphthol-3 : 6-disulphonate (36 g.) in water (120 c.c.) and 5N-sodium hydroxide (40 c.c.) was run in during 1 hr. Stirring was continued at 0° for 30 hrs. in all and then the red liquid was kept for 12 hrs., warmed at 50° for 1 hr., exactly neutralised with sodium carbonate, evaporated to small volume, and cooled, and 10N-sulphuric acid (20 c.c.) added. After standing on ice for several days the acid sodium salt was collected and converted into the *trisodium* salt, which was recrystallised several times from boiling water and obtained as a black powder very soluble in water (Found: I, 31·8. $C_{16}H_8O_{10}N_2I_2S_2Na_2$ requires I, 30·9%).

Sodium 5 : 5′-*Di-iodo*-2 : 2′-*disulphodiphenyl*-4 : 4′-*bis*-[2″-*azo*-8″-*amino*-1″-*hydroxy*-3″ : 6″-*disulphonaphthalene*-7″-(*azo*-2‴ : 6‴-*di-iodobenzene*-4‴-*sulphonate*)] (B).—To a solution of sodium di-iodobenzidinedisulphonate (13 g.) and sodium nitrite (2·9 g.) in water (110 c.c.) in a freezing mixture, 5N-hydrochloric acid (40 c.c.) was slowly added; the tetrazonium salt formed a light orange suspension. After being stirred for 1 hr., this was added slowly to an ice-cold solution of the foregoing monoazo-dye (33 g.) in water (120 c.c.) and 5N-sodium hydroxide (100 c.c.). Stirring at a low temperature was continued for 6 hrs., a little octyl alcohol being used to prevent frothing. After standing overnight, the dark maroon-red liquid was warmed at 50° for 1 hr., and the acid sodium salt (22 g.) isolated as above described. A solution of this in the minimal amount of boiling water and sodium carbonate (2 g.) was evaporated to small volume; the *octasodium* salt of the tetrakisazo-dye was obtained as a black powder (8 g.), extremely soluble in water, yielding a deep brown-red solution. For analysis it was dialysed and recrystallised from water (Found: I, 32·3; Na, 8·6. $C_{44}H_{18}O_{26}N_{10}I_6S_6Na_8$ requires I, 33·1; Na, 8·0%).

4 : 6-*Di-iodoanthranilic Acid* (compare Wheeler and Johns, *Amer. Chem. J.*, 1910, **43**, 405).—A solution of sodium anthranilate (31·8 g.) in water (200 c.c.) at 60° was added during 1 hr. to a stirred solution of iodine chloride (80 g.) in water (350 c.c.) and hydrochloric acid (150 c.c.) also at 60°. The mixture, which rapidly threw down a dark precipitate, was stirred for 3 hrs. at 70—80°, kept overnight, and filtered. The brown residue was dissolved in dilute sodium hydroxide solution (charcoal) and precipitated with an excess of hydrochloric acid in the presence of a small quantity of sodium sulphite to remove free iodine. Recrystallisation from a large volume of alcohol gave di-iodoanthranilic acid (51 g.) in light brown, felted needles, m. p. 228—230° (Found: I, 65·5. Calc.: I, 65·3%).

Sodium 2-(2′ : 4′-*Di-iodo*-6′-*carboxybenzeneazo*)-1-*amino*-8-*naphthol*-3 : 6-*disulphonate*.—Di-iodoanthranilic acid (19·6 g.) in warm water (360 c.c.) and 5N-sodium hydroxide (10 c.c.) was stirred in an ice-bath, and sodium nitrite (3·6 g. in aqueous solution) added, followed by 5N-hydrochloric acid (40 c.c.); the diazonium chloride formed a yellow suspension. After 2 hrs. an ice-cold solution of sodium hydrogen 1-amino-8-naphthol-3 : 6-disulphonate (18·2 g.), in water (100 c.c.) and 5N-sodium hydroxide (20 c.c.) was slowly added, and stirring continued at 0° for 30 hrs. and at 30—40° for 3 hrs. The dark maroon liquor was centrifuged, and the slurry drained (pump) and dissolved in boiling water (80 c.c.) and sodium carbonate (5 g.). The bright red solution was filtered, evaporated to small volume, and chilled; the *monoazo-dye* was obtained in micro-needles (14 g.); recrystallisation from water gave the pure dye (Found: I, 31·6. $C_{17}H_8O_9N_2I_2S_2Na_2$ requires I, 32·3%).

Sodium 5 : 5′-*Di-iodo*-2 : 2′-*disulphodiphenyl*-4 : 4′-*bis*-[2″-*azo*-8″-*amino*-1″-*hydroxy*-3″ : 6″-*disulphonaphthalene*-7″-(*azo*-2‴ : 4‴-*di-iodobenzene*-6‴-*carboxylate*)].—The foregoing monoazo-dye (31 g.; 2 mols.) was coupled in alkaline solution with 1 mol. of tetrazotised sodium di-iodobenzidinedisulphonate (13 g.) in the manner described for the analogue above. The product, isolated in a similar manner, gave the *tetrakisazo-dye* as a maroon-black microcrystalline powder soluble in water with production of brown-red solutions (Found: I, 33·3; Na, 8·0. $C_{46}H_{18}O_{34}N_{10}I_6S_6Na_8$ requires I, 34·0; Na, 8·2%).

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152. *Isethionic Acid.*

By ALAN A. GOLDBERG.

A new method of preparation of isethionic acid and its salts is described together with some sodium *O*-acylisethionates.

ISETHIONIC acid, $CH_2(OH)\cdot CH_2\cdot SO_3H$, has been prepared by the action of solid sulphur trioxide on ethyl alcohol (Magnus, *Annalen*, 1833, **6**, 163; *Ann. Physik*, 1839, **47**, 509), on ethyl hydrogen sulphate (Meves, *Annalen*, 1867, **143**, 196), and on diethyl ether (Hübner, *ibid.*, 1884, **223**, 210), by the interaction of ethylene or ethyl alcohol with sulphur trioxide dissolved in liquid sulphur dioxide (F.P. 716,914; B.P. 378,895), by the action of aqueous sodium hydrogen sulphite on ethylene chlorohydrin at 180° (Collmann, *Annalen*, 1868, **148**, 107) and by the passage of ethylene oxide into aqueous sodium hydrogen sulphite, giving the sodium salt in good yield (Lauer and Hill, *J. Amer. Chem. Soc.*, 1936, **58**, 1873; Rumpf, *Bull. Soc. chim.*, 1938, **5**, 877).

Since difficulties are encountered in working with sulphur trioxide, and ethylene oxide is not always accessible, a new method has been found in the reaction between ethyl sulphate and fuming sulphuric acid at a low temperature with production of ethyl hydrogen sulphate and ethionic acid; when the product is boiled with water, these compounds are hydrolysed, the former into sulphuric aicd and alcohol and the latter into sulphuric acid and isethionic acid. By removing the sulphuric acid as calcium sulphate the calcium salt of isethionic acid may be obtained easily and in excellent yield; other salts can be produced by double decomposition in aqueous solution.

Sodium *O*-acylisethionates are obtained by heating acyl chlorides with finely divided anhydrous sodium isethionate with or without a neutral diluent such as xylene. They are extremely soluble in water and are hydrolysed very slowly at the neutral point, more rapidly at low p_H values, and very rapidly in strongly alkaline solutions. Long-chain acylated isethionic acids in the form of their sodium salts have been used as wetting agents and detergents which function in acid liquors (B.P. 366,916). Because of the high solubility of sodium acylisethionates and their ability to hydrolyse into the corresponding acyl acid and the relatively non-toxic sodium isethionate, the latter would appear to possess desirable properties as a solubilising group for therapeutically active insoluble organic acids which may not be used in the form of their sodium salts owing to immediate precipitation by the gastric juice of the insoluble free carboxylic acid. It would, in addition, appear probable that the esterification of the carboxylic acid with sodium isethionate inhibits to some extent the normal detoxifying process occurring in the liver and kidney of conjugating the carboxylic acid with glycine which results not only in detoxification but in loss of therapeutic activity. *Sodium* O-*phenylacetylisethionate*, *sodium* O-β-*phenylpropionylisethionate* and *sodium* O-*acetylmandelylisethionate* have been prepared for examination as urinary disinfectants when administed by the oral and intravenous routes; the pharmacological results will be published separately.

The median lethal dosages (LD_{50}) recorded are for a single subcutaneous injection into 6—8 weeks old white mice weighing 20—24 g.

Experimental.

Calcium Isethionate.—Fuming sulphuric acid containing 60% of free sulphur trioxide (150 g.; 77 c.c.) was added during 2½ hours with slow stirring to ethyl sulphate (100 g.; 85 c.c.) in a strong freezing mixture at such a rate that the temperature did not exceed 10°. After standing overnight at room temperature, the dark liquid was poured into water (1 l.) and refluxed for 10—12 hours. Calcium carbonate (150 g.) in the form of a thin milk with water was added, and the calcium sulphate separated and washed with boiling water. The acid filtrate and the washings were evaporated to *ca.* 1 l. and refluxed for 10—12 hours in order to complete the hydrolysis of the ethyl hydrogen sulphate and ethionic acid. Calcium carbonate (50 g.) was then added, the calcium sulphate removed and washed with boiling water, the combined filtrates and washings evaporated, and the calcium sulphate which crystallised removed (charcoal) by filtration (*). The filtrate was evaporated on the water-bath to *ca.* 110 c.c. and kept on ice for 12 hours; it then set to a semi-solid crystalline mass of calcium isethionate, which was well drained (pump). The filtrate was further evaporated, seeded, and kept on ice; the further heavy crop of calcium isethionate obtained was drained. The combined crops were dehydrated on the water-bath in a vacuum, pure anhydrous calcium isethionate (118 g.) being obtained as a fine white powder. The mother-liquor from the second crop was still rich in calcium isethionate. A sample was recrystallised from the minimum amount of boiling water and separated into two fractions (i) and (ii), which were dehydrated at 115°/5 mm., for 3 hours [Found : Ca, (i) 13·7, (ii) 13·6. Calc. for $C_4H_{10}O_8S_2Ca$: Ca, 13·8%]. 10 Parts of calcium isethionate dissolve in 16 parts of water at 25° and in just less than 10 parts at 100°.

Barium Isethionate.—In order to test more thoroughly the homogeneity of the product of the above reaction, one preparation (from 100 g. of ethyl sulphate) was converted into the barium salt by using the equivalent amount of barium carbonate in place of calcium carbonate for removal of the sulphuric acid. Barium isethionate has a much steeper solubility curve than has the calcium salt and therefore lends itself better to fractional crystallisation. The barium isethionate isolated (143 g.) was dissolved in boiling water (220 c.c.) and separated by fractionation into four fractions : (i) 9 g., (ii) 61 g., (iii) 39 g., and (iv) 25 g. The first two fractions were dehydrated at 120°/5 mm. for 3 hours and analysed as such and the last two fractions were recrystallised separately, dehydrated, and analysed [Found : Ba, (i) 35·3, (ii) 35·4, (iii) 35·3, (iv) 35·0. Calc. for $C_4H_{10}O_8S_2Ba$: Ba, 35·5%].

Potassium Isethionate.—To the solution of calcium isethionate obtained above (*) from 100 g. of ethyl sulphate, potassium carbonate (*ca.* 70 g.), dissolved in water, was added in portions until further small additions caused no more precipitation of calcium carbonate. The precipitate was removed, and the filtrate evaporated to a very small volume and cooled; the potassium isethionate then obtained in stout white needles was dehydrated at 110°/5 mm. (130 g.) (Found in recrystallised anhydrous salt : K, 23·8; S, 19·3. Calc. for $C_2H_5O_4SK$: K, 23·8; S, 19·5%). Potassium isethionate is much less hygroscopic than the sodium salt. 10 Parts of it dissolve in 12 parts of water at 25° and in less than 6 parts at 100°.

Sodium Isethionate.—This was obtained in small white tablets in the same manner as the potassium salt by using sodium carbonate (54 g.) in the place of potassium carbonate (70 g.). The yield of anhydrous sodium isethionate from 100 g. of ethyl sulphate was 111 g. (Found : Na, 15·4; S, 21·3. Calc. for $C_2H_5O_4SNa$: Na, 15·5; S, 21·6%). The median lethal dose is 8·8 g./kg. Sodium isethionate is hygroscopic and is rather more soluble than the potassium salt.

Sodium O-*Phenylacetylisethionate.*—An intimate mixture of anhydrous sodium isethionate (14·8 g.) and phenylacetyl chloride (17·0 g.) was heated at 130—140° (oil-bath) until no more hydrogen chloride was evolved (4 hours). The dark yellow oil was dissolved in boiling water (100 c.c.), filtered (charcoal), and extracted with ether to remove phenylacetic acid. The aqueous liquor was adjusted to p_H 7·2 with sodium hydroxide and evaporated under reduced pressure until incipient crystallisation took place. On cooling, it set to a white semi-solid mass, which was drained (pump) and recrystallised from boiling water (20—25 c.c.); *sodium* O-*phenylacetylisethionate* was then obtained (10·0 g.) in stellate clusters of white needles (Found in salt dehydrated at 100°/5 mm. : S, 12·2. $C_{10}H_{11}O_5SNa$ requires S, 12·0%). Median lethal dose, 3·3 g./kg. (LD_{50} of phenylacetic acid, 1·7 g./kg.).

Sodium O-β-*Phenylpropionylisethionate.*—β-Phenylpropionyl chloride (27 g.), anhydrous sodium isethionate (21 g.), and xylene (75 c.c.) were refluxed (140°) until no more hydrogen chloride was evolved (4 hrs.). The hot liquor was filtered and the residue was washed with a little ether, dissolved in boiling water (50 c.c.), filtered (charcoal), and kept on ice. The white crystalline precipitate, recrystallised from boiling water (30 c.c.), gave *sodium* O-β-*phenylpropionyl-*

isethionate (14 g.) in white flakes (Found in dehydrated salt: S, 11·1. $C_{11}H_{13}O_6SNa$ requires S, 11·4%). Median lethal dose, 2·0 g./kg. (LD_{50} for β-phenylpropionic acid, 1·1 g./kg.).

Sodium O-Acetylmandelylisethionate.—This was obtained in good yield in the same manner from acetylmandelyl chloride (*Org. Syn.*, **4**, 1) (21·2 g.), sodium isethionate (14·8 g.), and xylene (75 c.c.). It was extremely soluble in cold water and was obtained analytically pure only with difficulty by crystallisation from dilute methanol (Found in dehydrated salt: S, 9·4. $C_{12}H_{13}O_7SNa$ requires S, 9·9%). Median lethal dose, 6·5 g./kg. (LD_{50} for acetylmandelic acid, 5·5 g./kg.).

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153. *Interaction of* p-*Cresol and other Phenols with Chloral and its Hydrate.*

By MICHAEL P. BALFE and WILLIAM C. WEBBER.

In the course of an investigation which we have had to discontinue before completion, compounds of type (I) have been prepared from phenol and *p*-cresol by interaction with chloral. (II, X = Me) was prepared by Pauly and Schanz (*Ber.*, 1923, **56**, 979) from *p*-cresol and chloral hydrate; an improved preparation is now described. Acetylated derivatives of (II), (III), (IV), and (V), all of which are primarily derived from *p*-cresol and chloral or chloral hydrate, are described.

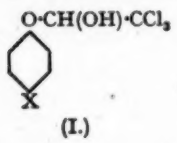
Phenols which contain electron-attracting *p*-substituents do not yield compounds of these types, but give only benzdioxin derivatives (VII) on reaction with chloral (Chattaway *et al.*, J., 1927, 685, 2013; 1928, 1088). The mechanism of this reaction is discussed.

EQUIMOLECULAR proportions of *p*-cresol and chloral react at room temperature, yielding a moderately stable p-*tolyl ether* (I, X = Me); the reaction is accelerated by a trace of anhydrous potassium carbonate. A less stable *phenyl ether* (I, X = H) can also be prepared, but under these conditions chloral does not react with *o*- or *m*-cresol, *p*-nitrophenol or *p*-hydroxybenzoic acid.

We find that (II, X = Me) is best prepared by repeated saturation of a melt of *p*-cresol and chloral hydrate with hydrogen chloride. Its diacetyl derivative was described by Meldrum and Lonkar (*J. Univ. Bombay*, 1937, 116) and we have now obtained a *monoacetyl* derivative. Though this gives colorations (fugitive on heating) with ferric chloride solution, this reaction is not always diagnostic of phenolic groups (*e.g.*, acetoacetic ester and lactic acid give colorations, but thymol does not; see also the discussion on this point by Raschig, *Z. angew. Chem.*, 1907, **20**, 206). We conclude that the phenolic group is acetylated, because the compound is insoluble in cold aqueous sodium hydroxide, and gives the monoacetyl derivative of (III, X = Me) by interaction with *p*-cresol.

On addition of concentrated sulphuric acid to an equimolecular mixture of (II, X = Me) and *p*-cresol in acetic acid solution, much resinification and sulphonation occur, but three derivatives can be isolated. These are the above-mentioned monoacetyl derivatives of (II) and of (III) and a diacetyl derivative of (IV). We have not determined which of the two possible diacetyl derivatives of (IV) we have obtained, but the composition of the substance is indicated by its conversion into the *triacetyl* derivative of (IV).

On treatment with aqueous potassium hydroxide (3 mols.), (II, X = Me) yields a *substance* $C_{15}H_{15}O_4Cl_3$, m.p. 184°. It is insoluble in cold aqueous sodium hydroxide, and on acetylation yields a substance $C_{22}H_{19}O_6Cl_3$; we therefore suggest that its constitution is (V) (the isomers of which are less probable), the acetylation product being a *diacetate*. Meldrum and Lonkar (*loc. cit.*) obtained a substance, m. p. 182°, of the same chlorine content as (V) by treating (II, X = Me) with sodium hydroxide (10 mols.). They concluded that it was (VI) with one molecule of ethyl alcohol of crystallisation. Our compound does not contain ethyl alcohol, but whether that obtained by Meldrum and Lonkar's method is identical with it, or is its precursor, cannot be stated, since we have not repeated the experiment by their method.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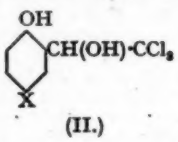
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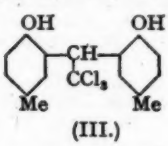
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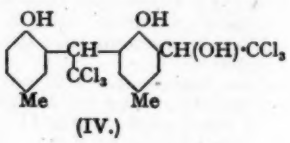
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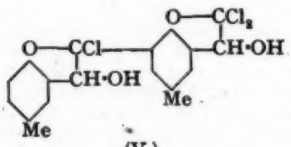
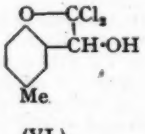
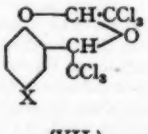

(V.)


(VI.)


(VII.)

The formation of (II) from *p*-cresol is slow, and when X is electron-attracting (NO_2, CO_2H), this reaction does not occur under the conditions which we used. Thus neither (I) nor (II) can be obtained from phenols which contain an electron-attracting *p*-substituent, yet both modes of reaction must occur during the formation

of the benzdioxin derivative (VII) from such phenols and chloral in the presence of sulphuric acid (Chattaway *et al.*, *loc. cit.*). This reaction probably occurs in the following stages: (i) the chloral is converted into a kationic entity, the reactivity of which overcomes the deactivating effect of the *p*-substituent in the phenol, and an intermediate of type (II) is formed; (ii) ionisation of the phenol, repressed by the sulphuric acid, is now assisted by the second electron-attracting substituent. A small equilibrium proportion of phenoxide * molecules, substituted both as in (I) and as in (II), can therefore exist; these are immediately converted into (VII) by the sulphuric acid and the process therefore goes to completion. This scheme differs slightly from that suggested by Chattaway (J., 1926, 2720), but his initial stage, formation of (I), followed by rearrangement to (II), appears to be ruled out by the fact that a compound of type (II) can be obtained from anisic acid (Chattaway and Calvet, J., 1928, 1088).

In the course of this work, we have observed the separation of a compound of chloral and sulphuric acid, from mixtures of chloral or its hydrate and sulphuric acid in somewhat narrow ranges of composition and of strength of acid. Its composition probably corresponds to $CCl_3\cdot CH(OH)\cdot O\cdot SO_2\cdot OH, 1\frac{1}{2}H_2O$, resembling chloral hydrochloride (Vorländer, *Annalen*, 1905, **341**, 21). This substance may be the alkyl hydrogen sulphate corresponding to the sodium salt described by Kerp and Bauer (*Chem. Ztg.*, 1907, **31**, 970).

Experimental.

p-Tolyl ββδ-Trichloro-α-hydroxyethyl Ether (I, X = Me).—Powdered anhydrous potassium carbonate (0·5 g.) was added during 1½ minutes to a solution of *p*-cresol (10·8 g.; 1 mol.) in a mixture of chloral (14·8 g.; 1 mol.) and chloroform (5 c.c.). After 3 minutes the mixture had crystallised. The solid was collected, washed with 100 c.c. of light petroleum (b. p. 60—80°) containing 5% of benzene, and recrystallised from methylene chloride (15 c.c.) at 0°, giving the *ether* (I, X = Me) (9 g., 35% yield) in large, thick, regular, hexagonal plates, m. p. 46—47° (Found: C, 42·2; H, 3·5. $C_9H_9O_2Cl_3$ requires C, 42·2; H, 3·5%). When anhydrous sodium acetate (5 g.) was used instead of potassium carbonate, the yield was 6 g. The crystalline compound was unchanged after storage in the absence of moisture for 2 years, and 10 g. of the compound, mixed with 0·2 g. of potassium carbonate, 0·2 g. of magnesium carbonate, or 0·5 g. of anhydrous potassium acetate, were unchanged after 27 months. It was also recovered unchanged after storage in solution in benzene or chloroform for 2 years. It could not be recovered from solution in methyl or ethyl alcohol or acetone. On fractional distillation 20 g. of the compound yielded 11·2 g. of chloral (b. p. 97—98°) and 0·3 g. of chloral hydrate. Its chloral content was determined by decomposition with standard potassium hydroxide and back-titration of the excess of alkali: 0·2968 g. neutralised 9·7 c.c. of 0·8602*N*-alkali; hence chloral content = 57·4% ($C_9H_9O_2Cl_3$ requires 57·7%).

Phenyl ββδ-trichloro-α-hydroxyethyl ether (I, X = H), prepared by the same method, chloral (29·6 g.; 1 mol.) and phenol (18·8 g.; 1 mol.) being used with anhydrous potassium carbonate (1 g.), formed large, colourless, rhombic plates, m. p. 15—18° (yield 3·6 g., 7·5%), chloral content 60% ($C_8H_7O_2Cl_3$ requires 63·7%). The analysis and m. p. range reflect the lesser stability of the compound, which decomposes more readily in solution than the *p*-tolyl ether.

3-ββδ-Trichloro-α-hydroxyethyl-p-cresol (II, X = Me).—Hydrogen chloride was bubbled intermittently through a melt of chloral hydrate (33·1 g.; 1 mol.) and *p*-cresol (21·6 g.; 1 mol.) with occasional shaking. The crystals which separated were removed after approximately 6-day intervals, three crops (18, 10, and 7 g.; total yield, 35%) being obtained; no by-products could be isolated from the mother-liquors. A similar result was obtained when chloral was used instead of its hydrate.

(I, X = Me) is converted into (II) when it is stored in an atmosphere of hydrogen chloride for several months, or kept in solution in the presence of potassium carbonate; this change probably occurs *via* dissociation of (I) into its components, rather than ionic rearrangement, since it is retarded by addition of *p*-cresol.

The compound (II, X = Me) crystallises from much boiling water or from light petroleum (b. p. 60—80°) containing 10% of benzene in colourless needles, m. p. 147·5° (Found: Cl, 41·7. Calc. for $C_9H_9O_2Cl_3$: Cl, 41·9%), very soluble in ethyl alcohol and acetic acid, less soluble in ether, chloroform or benzene. It gives a deep magenta coloration with concentrated sulphuric acid; with ferric chloride solution, a dark blue colour in 40% aqueous ethyl alcohol and a deep green coloration in 30% aqueous methyl alcohol. On simultaneous hydrolysis and oxidation with potassium dichromate (Jeneff's method) it yields 5-methylsalicylaldehyde, m. p. 55°, in 10% yield (Found: C, 70·6; H, 5·9. Calc. for $C_8H_8O_2$: C, 70·6; H, 5·9%) (Tiemann and Schotten, *Ber.*, 1878, **11**, 773, give m. p. 56°).

The diacetyl derivative (acetic anhydride–sodium acetate) has m. p. 104·5° (Meldrum and Lonkar, *loc. cit.*, gave m. p. 106°) and crystallises in clusters of colourless monoclinic columns from acetic acid and as slender columns from aqueous alcohol (Found: Cl, 31·5. Calc. for $C_{13}H_{13}O_4Cl_3$: Cl, 31·4%). The *monoacetyl* derivative was obtained by saturating a solution of (II) (2 g.) in glacial acetic acid (30 c.c.) with hydrogen chloride and after 24 hours pouring it into water; recrystallised from light petroleum (b. p. 60—80°) containing 10% of benzene, the monoacetate formed colourless needles, m. p. 168° (yield, 66%) (Found: C, 44·2; H, 4·0; Cl, 35·6. $C_{11}H_{11}O_3Cl_3$ requires C, 44·4; H, 3·7; Cl, 35·8%).

Monoacetyl Derivative of (III, X = Me).—To a solution of 14·8 g. (1 mol.) of the monoacetyl derivative of (II, X = Me) and 5·4 g. (1 mol.) of *p*-cresol in 250 c.c. of glacial acetic acid, 180 g. of 99% sulphuric acid were added, with stirring, at a rate to maintain the temperature at 50°. The clear solution was poured into 1 l. of water, and the precipitate washed with much water, then recrystallised three times from aqueous alcohol. The resulting *monoacetate* of (III, X = Me) had m. p. 198°. Yield, 4·5 g. (23%) (Found: C, 55·7; H, 4·3; Cl, 27·6. $C_{18}H_{17}O_3Cl_3$ requires C, 55·8; H, 4·4; Cl, 27·5%). On boiling with acetic anhydride and sodium acetate, it gave the *diacetyl* derivative of (III), m. p. 162° (Found: Cl, 24·4. $C_{20}H_{19}O_4Cl_3$ requires Cl, 24·7%). In a similar experiment using 12·8 g. (1 mol.) of (II) and 7·5 g. (1 mol.) of *p*-tolyl acetate, 11% of the monoacetyl derivative of (III) and 10% of its diacetyl derivative were obtained.

Interaction of (II, X = Me) *and* p-*Cresol in Acetic Acid Solution in Presence of Sulphuric Acid.*—Below 20°, only slow sulphonation and above 60°, condensation to uncrystallisable derivatives, occurred. Between 50° and 60°, small amounts of crystallisable derivatives were formed; *e.g.*, to 12·8 g. of (II, X = Me) and 5·4 g. of *p*-cresol (1 mol.) in 300 c.c. of glacial acetic acid, 180 g. of 99% sulphuric acid were added, the temperature being kept at 60°. The cooled mixture was poured into 1 l. of water, and the precipitate washed with much water, dried, washed with 50 c.c. of light

* The formation of these hemi-acetals is a reversible process, and involves ionisation of the hydroxyl group. Like that of the other compounds (acetals and *gem*-diols) of the general formula R′·CH(OR″)·OR‴, their stability increases with increasing electron attraction in R′, and decreases with increasing electron-release from OR″ and with increasing electron attraction (anionic stability) in OR‴.

petroleum (b. p. 60—80°), and recrystallised from aqueous alcohol, being separated into the monoacetyl derivative of (II, X = Me) (2·1 g.), the monoacetyl derivative of (III) (0·5 g.), and a diacetyl derivative of (IV) (approx. 0·1 g.), m. p. 200°.

Interaction of (II, X = Me) *and* p-*Cresol in Nitrobenzene Solution in Presence of Sulphuric Acid.*—To 12·8 g. of (II, X = Me) and 10·8 g. (2 mols.) of *p*-cresol in 60 c.c. of nitrobenzene, 18 g. of 99% sulphuric acid in 20 c.c. of nitrobenzene were added, the temperature being kept at 15°. The mixture was then poured into water, steam-distilled to remove *p*-cresol and nitrobenzene, and evaporated to dryness, leaving a resinous mass (15·6 g.). Higher temperature, higher proportions of sulphuric acid, or use of undiluted sulphuric acid, produced only water-soluble sulphonation products (*p*-cresolsulphonic acid was isolated as its ammonium salt). Use of 90% sulphuric acid produced no reaction.

A similar resinous product was obtained in experiments as above with (II, X = Me), without *p*-cresol. These resinous products were dissolved in glacial acetic acid and saturated with hydrogen chloride. From the gum which separated, after lixiviation with methyl alcohol and repeated crystallisation from ethyl alcohol, a *diacetyl* derivative of (IV) was obtained (approx. 1 g.), in nodular clusters of colourless needles, m. p. 200° (slight decomp.) (Found: C, 45·7; H, 3·5; Cl, 36·8. $C_{22}H_{20}O_6Cl_6$ requires C, 45·7; H, 3·5; Cl, 36·9%).

This diacetyl derivative (on acetylation with acetic anhydride) and the above resinous products (on boiling with acetic anhydride and sodium acetate) gave the *triacetyl* derivative of (IV), crystallising from ethyl alcohol in short colourless prisms, m. p. 178° (Found: C, 46·5; H, 3·7; Cl, 34·2. $C_{24}H_{22}O_6Cl_6$ requires C, 46·5; H, 3·5; Cl, 34·4%). The resinous products gave a 6% yield of triacetate.

Action of Potassium Hydroxide on (II, X = Me).—To a solution of 12·8 g. of (II, X = Me) in 50 c.c. of water containing 2·8 g. (1 mol.) of potassium hydroxide at 16°, 100 c.c. of water containing 5·6 g. of potassium hydroxide were added slowly, with stirring. The orange-red precipitate was twice recrystallised from benzene, finally from aqueous alcohol (yield, 0·8 g.). This *substance*, m. p. 184°, is insoluble in aqueous alkali, indicating that it is not highly hydroxylated, and its analysis (Found: C, 54·0; H, 3·8; Cl, 26·5. $C_{18}H_{15}O_4Cl_3$ requires C, 53·8; H, 3·7; Cl, 26·5%) corresponds with formula (V). On boiling with acetic anhydride and sodium acetate, it yields a *diacetate*, crystallising from ethyl alcohol in clusters of colourless rhombs, m. p. 133° (Found: C, 54·6; H, 4·0; Cl, 22·0. $C_{22}H_{19}O_6Cl_3$ requires C, 54·4; H, 3·9; Cl, 21·9%).

Chloral Hydrogen Sulphate.—Chloral hydrate (16·55 g. portions) was stirred with sulphuric acid (100 g.) of various strengths for 6 hours, and the crystalline mass which formed the upper layer was collected after 2 days. From acid of 77% strength or lower, no crystals separated (except a deposit of unchanged chloral hydrate); the maximum yield (22 g.) was obtained with 79·8% acid, and higher strengths of acid gave lower yields (16 g. at 81·2% strength). At any given acid strength between 78·5 and 80·5% there is an optimum ratio of chloral to acid. Thus from 49·65 g. of chloral and 78·5% acid, the maximum yield (48 g.) was obtained with 500 g. of the acid; chloral (44·24 g.) gave 62 g. of the crude substance on mixing with 300 g. of 77·0% acid. The substance absorbed moisture when exposed to air, yielding chloral hydrate and sulphuric acid, and on heating decomposed, chloral and sulphuric acid separating in two layers.

The substance separates in a pulpy mass of small needles. Between 16° and 22°, it appears to be in equilibrium with acid of composition $H_2SO_4,1\frac{1}{2}H_2O$. Accurate analysis is impossible, as it decomposes when washed to remove adhering acid. An attempt was made roughly to estimate its composition by determining the sulphate (as barium sulphate) and the chloral + sulphuric acid (titration with sodium hydroxide) in the filtrate from a known weight of the substance obtained from known amounts of chloral hydrate and sulphuric acid. The composition of the solid corresponded to $CCl_3{\cdot}CH(OH){\cdot}SO_3{\cdot}OH,1\frac{1}{2}H_2O$ + 21·2% of $H_2SO_4,1\frac{1}{2}H_2O$. Since the solid could not be freed from surplus acid, the result suggests that it contains chloral and sulphuric acid in equimolecular proportion.

Thanks are due to Dr. J. Kenyon, F.R.S., for his interest in this work.

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154. *An Interpretation of the Sandmeyer Reaction. Part III. Further Evidence in favour of a Mechanism involving Anionoid Halogen.*

By HERBERT H. HODGSON, STANLEY BIRTWELL, and JOHN WALKER.

Catalysed decompositions of diazonium kations are produced by anionoid complexes; the efficiency of complexes with metals other than cuprous copper appears to be dependent on the degree of positivity of the kation. This point of view, expressed in Part I, is emphasised by further experimental data.

OUR recent interpretation of the Sandmeyer reaction (J., 1941, 770), based on work commenced in 1931, indicated a mechanism whereby stable halogen ions were rendered exceedingly reactive by labile combination with cuprous salts to form anionoid complexes, the catalytic function of the cuprous salt being to destabilise the halogen octet. This interpretation was subsequently extended to explain the similar catalytic action of cupric salts, and it provides a rational explanation for all halogen replacements of the diazonium group whether in aqueous or other media, or in the dry state. The decomposition of diazo-perbromides can only be explained by such an anionoid mechanism.

Discussion of Waters' Complex Cuprous-Kation Theory (this vol., p. 266).—Waters' suggested mechanism, which is almost identical with that for the reduction of a diazonium compound to a diaryl, is based on his statement that we have " not been able to suggest why the *cuprous* double salts decompose in a way which is so very different from the double salts which diazonium halides readily form with the halides of other metals, such as zinc," *i.e.*, " the unique character (p. 267) of cuprous salts as catalysts " for the Sandmeyer reaction. The term " unique " is modified by Waters to " *almost* unique " in the summary and on p. 270.

We must reaffirm emphatically that, far from being unable to suggest why cuprous salts were *almost* unique as Sandmeyer catalysts, we held the belief (implicit in the very first paragraph of our paper, *loc. cit.*) that there was no justification for such a point of view as that now advanced by Waters, and in support thereof we quoted examples in both the benzene and the naphthalene series where cupric salts act as efficiently

(or nearly so) as cuprous salts, *i.e.*, examples for which the Waters explanation can have no validity whatever (cf. Waters, *loc. cit.*, p. 268). Moreover, Waters does not mention these reactions (Hodgson *et al.*, p. 772), although it is obvious that if cupric salts can behave under identical circumstances like cuprous salts, his whole argument for an oxidation–reduction mechanism involving a complex kation of a cuprous–diazonium double salt becomes invalid (cf. also, the antithesis to his claim, p. 267, for avoiding special structural formulæ for intermediate reaction complexes). In like manner, Sandmeyer's own statement that cupric salts were without the same action as cuprous salts was based on insufficient evidence.

We have previously pointed out (*loc. cit.*, p. 772) that the Sandmeyer reaction appears to be dependent on the degree of positivity of the diazonium ion, which, when of sufficient magnitude, enables the more ephemeral cupric halogen complexes to react like their more abundant cuprous analogues. This dependence is now further illustrated by the data for decompositions by cupric salts (see Table IV), which indicate that when the significant carbon has only a relatively small positive charge (as in diazotised aniline or *p*-toluidine), the yield of chloro-compound is only small, but with increase of positivity, as in *p*-chlorobenzenediazonium chloride, and still more so in *p*-nitrobenzenediazonium chloride, due to the $(-I)$ inductive effects of the chloro- and the nitro-group respectively, yields as ample as those with cuprous chloride are obtained. Incidentally, but important for the argument, no diaryl formation was observed in the decompositions with cupric salts, the usual by-product being the corresponding phenol. Waters implicitly concedes this point, since he depicts (*loc. cit.*, p. 268, Fig. I) the positive centres of a complex kation of a cuprous–diazonium double salt as attracting each other, an attraction which could only result in electron release to the significant carbon of the aryl group when this is at a higher positive potential than the cuprous copper. We submit that attraction is far more likely to occur between the reactive anionoid centre of a complex anion (such as is generally acknowledged to be formed when cuprous salts dissolve in mineral acids) and the positive significant carbon, than between positive centres in a complex structure such as that depicted by Waters.

Halogen Replacements by Metallic Complexes other than those of Copper.—P. H. Groggins (" Unit Processes in Organic Syntheses," McGraw-Hill Book Co., New York and London, 1938, p. 199) states: " Copper is *not* the only metal that can *advantageously* be employed for the replacement of the diazo-group by halogen. When the precaution is taken to ensure a maximum concentration of chloride ions, saturated solutions of calcium chloride, zinc chloride, and zinc-ammonio chloride *often* give equally good results." Recent work also, by ourselves with C. K. Foster (this vol., p. 581), has shown that many complex double salts of diazonium compounds with zinc chloride of general formula $(ArN_2)_2ZnCl_4$ are decomposed *in solution* in molten phenol by a mechanism identical with that of the Sandmeyer reaction in water, to give up to 50% yields of chloro-compound, the anionoid phenol playing a rôle identical with that of anionoid water.

When the double salts of diazonium chlorides with lead tetrachloride are heated with alcohol, the diazo-group is replaced by chlorine (Chattaway, J., 1924, **125**, 1981), the reaction being analogous to the decomposition of the perbromides and indicating the function of the metal to be that of host for the formation of the reactive complex anion.

The Dual Rôle of Cuprous Compounds.—We consider that it is more rational to postulate distinct mechanisms, (1) for halogen substitution and (2) for diaryl formation, than a single mechanism such as that proposed by Waters for both. Hodgson and Walker found (J., 1932, 1620) that when the amount of water was reduced, *i.e.*, the concentration of the complex cuprous anion increased, diaryl formation could be prevented altogether in the decomposition of *o*- and *p*-nitrobenzenediazonium chlorides by cuprous chloride in hydrochloric acid solution. The Waters mechanism does not explain the complete absence of diaryl formation in such cases, which is due not to the high concentration of chlorine ions, since this may be very moderate, but to conditions which favour the maximum production of a complex anion. Likewise, when the water content was increased (cf. Hodgson *et al.*, *loc. cit.*, p. 776), the formation of diaryl (2) was also increased but was accompanied by that of nitrophenol, indicating that anionoid water now competed with the cuprous reducing agent for the diazonium salt.

The Waters mechanism, moreover, differs only in elaboration from that already proposed by Groggins (*op. cit.*, p. 199), who also introduces hydroxyl anions as competitors with the kationoid complex. We submit that it is more reasonable to assume competition for the diazonium kation between a complex cuprous anion and anionoid water (since there are no hydroxyl ions present in such strong acid solutions, in a realistic sense of the term), than to assume a competing cuprous kation. The fact that by reducing the amount of anionoid copper complex by dilution of the solution with water, the yield of halogen compound is decreased, whereas that of phenol is increased, supports our explanation.

Decompositions by Copper Sulphate, with and without other Oxidising Agents.—Reactions between nitroaryldiazonium sulphates, copper sulphate, and sodium chloride or bromide in sulphuric acid solution to give chloro- or bromo-aryls in 90—100% yields were discovered by Hodgson (*J. Soc. Dyers and Col.*, 1926, **42**, 365). Benzenediazonium sulphate itself has now been found to give a 38% yield of bromobenzene under similar conditions. To eliminate any chance of cuprous salt formation (cf. Waters, *loc. cit.*), a number of reactions have been carried out with *p*-nitrobenzenediazonium sulphate, copper sulphate, and sodium bromide, in the presence of ammonium persulphate and also of ferric chloride. Although the yields of halogeno-aryl were not much affected (see Table I), nevertheless in the ferric chloride experiment a mixture of about equal parts of 4-chloro- and 4-bromo-nitrobenzene resulted. When hydrogen peroxide was used as the supplementary oxidising agent, the yield of 4-bromonitrobenzene was reduced, and the reaction included the initial formation

of a yellow precipitate (probably of a perbromide), which, on heating, decomposed with evolution of bromine and separation of 4-bromonitrobenzene. The last experiment might suggest that when oxidising agents are present, bromine replacement occurs *via* intermediate formation of a perbromide, but in the decompositions with sodium bromide and copper sulphate alone, the by-product was always the corresponding phenol, which was never found to have been brominated. Further, a mixture of copper sulphate, sodium bromide, and phenol, in the presence of dilute sulphuric acid, gave no precipitate of tribromophenol, even when heated under reflux on the water-bath for an hour and subsequently kept for 24 hours. Initial formation of perbromide does not therefore take place in the copper sulphate and sodium bromide experiments, and the mechanism of decomposition of the diazonium salt is *via* a cupric-copper anionoid complex as originally suggested by Hodgson *et al.* (*loc. cit.*, p. 772).

Decompositions by Ferric Chloride and Cupric Chloride in Hydrochloric Acid Solution.—Experiments in which dilute sulphuric acid solutions of *p*-nitrobenzenediazonium sulphate were decomposed in the presence of ferric chloride alone, and also with copper sulphate and sodium chloride, gave results (see Table II) which indicated clearly the catalytic influence of the copper salt and of the chloride-ion concentration. In the decompositions of *p*-nitrobenzenediazonium chloride (see Table III), it is of interest that a 41% yield of 4-chloronitrobenzene was obtained in concentrated hydrochloric acid alone, and that in this acid only minor variations were produced by additions of antimony trichloride, stannic chloride, and aluminium chloride. Ferric chloride and cupric chloride, however, increased the yield to 63% and 73% respectively. The catalytic influence of these salts is thus clearly demonstrated, and in the case of cupric chloride an efficiency almost equal to that of cuprous chloride was obtained with the nitro-compounds.

Conclusions.—The experimental evidence proves: (1) Cuprous salts do *not* possess the unique (or almost unique) character claimed for them first by Sandmeyer and recently by Waters. (2) In cases where the diazonium kation possesses sufficient positivity, cupric salts can function with efficiencies comparable with those of cuprous salts. (3) Metals other than copper can form anionoid complexes with halogens which decompose in like manner to the copper salts. (4) The Sandmeyer reaction is an oxidation–reduction process involving an electrophilic diazonium kation and a nucleophilic (anionoid) halogen which is part of a cuprous copper complex. (5) There are no fundamental differences in the mechanism of formation of halogen compounds during the decompositions of complex salts of diazonium chlorides with cuprous chloride, cupric chloride, zinc chloride or any other chloride, including hydrogen chloride, in aqueous or other media; such differences as do occur, *e.g.*, in the distribution of yield, are due to differences in stability and concentration of the complex anion, whereby the competing action of anionoid water can become negligible (cuprous salts) or predominant (zinc salts). (6) All the reactions studied can be interpreted by the simple anionoid mechanism already proposed (Hodgson *et al.*, J., 1941, 770; this vol., p. 376).

Experimental.

The Effect of Oxidising Agents on the Replacement of the Diazo-group by Bromine by Means of Sodium Bromide and Copper Sulphate.—Finely powdered *p*-nitroaniline (11 g.) was added to a solution of sodium nitrite (5·6 g.) in sulphuric acid (40 c.c., *d* 1·84) at 30—40° and, after dissolution, the mixture was cooled and poured on ice. The solution of diazonium salt was filtered, made up to 280 c.c., and divided into four equal portions, each being therefore equivalent to 1/50 g.-mol. of diazotised *p*-nitroaniline. Four solutions were then made up of crystallised copper sulphate (5 g.) and sodium bromide (5 g.) in water (25 c.c.), to which different oxidising agents were added, followed by the diazo-solution (Table I). The four mixtures were refluxed on the water-bath for 15 minutes, decomposition then being complete (decomposition began at *ca.* 80°). The 4-bromonitrobenzene was isolated by steam-distillation.

Table I.

Oxidising agent.	Yield of halogen compound, g.	Yield of halogen compound, %	M. p. of steam-volatile compounds.
None	2·5	63	125—126°
Ammonium persulphate (2·5 g.)	2·5	63	,,
20 Vol. Hydrogen peroxide (20 c.c.)	1·7	43	,,
Ferric chloride (3·5 g.)	2·6	74	102 *

* This m. p. corresponds to a mixture of equal parts of 4-chloro- and 4-bromo-nitrobenzene. See Table II (Hodgson *et al.*, *loc. cit.*, p. 775).

Aniline (18·6 g.), dissolved in sulphuric acid (20 c.c., *d* 1·84) and water (200 c.c.), was diazotised below 10° by a solution of sodium nitrite (14 g.) in water (50 c.c.). The mixture was poured into a solution at 80° of crystallised copper sulphate (100 g.) and sodium bromide (100 g.) in water (400 c.c.), heated on the boiling water-bath for 30 minutes, and steam-distilled; bromobenzene (12 g., 38% yield) passed over.

Decomposition of Diazotised p*-Nitroaniline by Ferric Chloride, alone and with Additions.*—*p*-Nitroaniline (1/50 g.-mol.) was diazotised by the nitrosylsulphuric acid method above, and the solution decomposed under the same conditions as those given above.

Table II.

Decomposition reagent.	Yield of 4-chloronitrobenzene, g.	Yield of 4-chloronitrobenzene, %	M. p. of steam-distilled product.
Ferric chloride (7 g.) in water (25 c.c.)	0·5	16	80—83°
Ferric chloride (3·5 g.), crystallised copper sulphate (5 g.), and sodium chloride (5 g.) in water (25 c.c.)	2·0	64	,,
Ferric chloride (3·5 g.) and crystallised copper sulphate (5 g.) in water (25 c.c.)	1·9	60	,,

Replacement of the Diazo-group by Chlorine.—A solution of *p*-nitroaniline (22 g.) in hydrochloric acid (50 c.c., *d* 1·16) and water (75 c.c.), while still warm enough to prevent crystallisation, was diazotised by stirring into a mixture of aqueous sodium nitrite and ice (250 g.). The filtered solution was made up to 400 c.c. and divided into 8 portions of 50 c.c., which each contained 1/50 g.-mol. of diazonium salt. These portions were added to solutions of 1/25 g.-mol. of various salts dissolved in (*a*) water (25 c.c.) or (*b*) hydrochloric acid (50 c.c., *d* 1·16). The temperature during the addition was maintained at *ca.* 80° and the mixtures were subsequently heated under reflux on the water-bath at 90—95° for 45—60 minutes. The 4-chloronitrobenzene formed was isolated by steam-distillation.

TABLE III.

Addition for (*a*), 1/25 g.-mol. in water (25 c.c.).	Yield of 4-chloro-1-nitrobenzene, g.	%	Addition for (*b*), 1/25 g.-mol. in HCl (50 c.c., *d* 1·16).	Yield of 4-chloro-1-nitrobenzene, g.	%
None (solution boiled)	0·3	9·5	HCl only (solution heated)	1·3	41
Zinc chloride (5·5 g.)	0·3	9·5	Zinc chloride (5·5 g.)	1·3	41
			Antimony trichloride (9 g.)	1·0	32
Hydrated stannic chloride (14·0 g.).....	0·4	13	Hydrated stannic chloride(14·0 g.) ...	1·3	41
Hydrated aluminium chloride (10·7 g.)	0·45	14·5	Hydrated aluminium chloride (10·7 g.)	1·5	48
Ferric chloride (anhydrous) (6·5 g.) ...	1·1	35	Ferric chloride (anhydrous) (6·5 g.) ...	2·0	63
Hydrated cupric chloride (6·9 g.)	2·5	80	Hydrated cupric chloride (6·9 g.)	2·3	73

The temperatures at which these reactions were carried out were necessary for the decompositions to be rapid and complete, but when the solutions were kept at room temperature during long periods, as good and sometimes better yields were obtained; *e.g.*, the cupric chloride experiment of Table III, when carried out at room temperature for 96 hours before removal of the product, gave 2·5 g. (80% yield), and with a mixture of crystallised copper sulphate (10 g.) and sodium chloride (5 g.) instead of cupric chloride, 2·7 g. of 4-chloro-1-nitrobenzene (86% yield) were obtained.

Decompositions of Various Diazonium Salts by Cupric Chloride, and by Copper Sulphate and Sodium Chloride.—In the following experiments, the amines were diazotised in hydrochloric acid, the concentration being 1/25 g.-mol. in acid (12·5 c.c., *d* 1·16) and water (77·5 c.c.). The diazonium solutions were then stirred into the decomposition solutions, which contained two equivalents of copper (2/25 g.-mol.) in water (50 c.c.).

TABLE IV (All the data are calculated to the nearest 1%).

Amine diazotised.	G.-mol. taken.	Decomposed by crystallised copper sulphate (20 g.) and sodium chloride (10 g.) in water (50 c.c.). Yield of chloro-compound, g.	%	Decomposed by hydrated cupric chloride (13·8 g.) in water (50 c.c.). Yield of chloro-compound, g.	%
Aniline	0·2	3·9	17	3·8	17
p-Toluidine	0·2	4·2	17	4·2	17
p-Chloroaniline	0·04	4·0	68	3·6	61
m-Nitroaniline	0·04	5·1	81	5·0	80
p-Nitroaniline	0·04	5·6	89	5·6	89
o-Nitroaniline	0·04	5·1	81	5·0	80
2:4-Dinitroaniline	0·04	6·3	81	6·2	80

Remarks.—The larger amounts of aniline and *p*-toluidine were taken to ensure greater accuracy in estimating the yields of chloro-compound, and the diazonium solutions were decomposed by a solution of (1) copper sulphate (100 g.) and sodium chloride (50 g.), and (2) hydrated cupric chloride (69 g.), in water (250 c.c.).

The 2 : 4-dinitroaniline (6·7 g.) was diazotised by the special method described by Saunders ("The Aromatic Diazo-Compounds and Their Technical Applications," London, 1936, p. 10), in 60 c.c. of sulphuric acid, and the solution diluted to 175 c.c. before decomposition by cupric chloride. No increase in yield was obtained by saturating the diazonium solution with sodium chloride before the addition of the cupric chloride solution.

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155. *The Influence of the 5-Nitro-group on the Halogenation and Nitration of 5-Nitro-1-naphthylamine and of Some Related Naphthalides.*

By HERBERT H. HODGSON and HAROLD S. TURNER.

The 5-nitro-group favours halogenation and mercuration of 5-nitro-1-naphthylamine and some related naphthalides at the 2-position, and nitration at the 4-position.

5-NITRO-1-NAPHTHYLAMINE is readily monobrominated and monomercurated in the 2-position, but direct iodination in the presence of yellow mercuric oxide is unsatisfactory and the reaction of chlorine is very rapid and complicated. 5-Nitroaceto-1-naphthalide, however, was chlorinated simultaneously in the 2- and the 4-position and monochlorination was not detected. The restraining kationoid field effect of the 5-nitro-group thus promoted halogenation and mercuration at the 2-position. 5-Nitroaceto-1-naphthalide, however, was nitrated initially at the 4-position, and 5-nitro-*p*-toluenesulphon-1-naphthalide simultaneously at the 2- and the 4-position, even with nitric acid in amount sufficient for mononitration only (see Hodgson and Walker, J., 1934, 180, for the analogous nitration of *p*-toluenesulphon-1-naphthalide). That nitration favours 4-

rather than 2-substitution has analogy with the nitration of 1-nitronaphthalene itself, which occurs predominantly in the 8-position (Hodgson, *J. Soc. Dyers and Col.*, 1936, **52**, 369).

Experimental.

Chlorination of 5-Nitroaceto-1-naphthalide.—5-Nitro-1-naphthylamine (10 g.) was acetylated by boiling it for 10 mins. in a mixture of acetic anhydride (7 c.c.) and glacial acetic acid (100 c.c.), and the filtered solution was treated with chlorine on the boiling water-bath until crystals of 2 : 4-*dichloro-5-nitroaceto-1-naphthalide* began to separate (*ca.* 30 mins.). After cooling, the product (8 g.) was collected and washed with and crystallised from glacial acetic acid; it formed colourless needles, m. p. 235·5° (Found : N, 9·4. $C_{12}H_8O_3N_2Cl_2$ requires N, 9·4%). Hydrolysis with boiling 50% sulphuric acid (80 c.c.) and ethyl alcohol (100 c.c.) gave 2 : 4-*dichloro-5-nitro-1-naphthylamine* (5·6 g.), which crystallised from aqueous ethyl alcohol in bright orange needles, m. p. 116·5° (Found : N, 11·1. $C_{10}H_6O_2N_2Cl_2$ requires N, 10·9%).

2 : 4-*Dichloro-5-nitronaphthalene.*—A solution of the above amine (2 g.) in glacial acetic acid (15 c.c.) was stirred into nitrosylsulphuric acid (0·8 g. of sodium nitrite and 10 c.c. of sulphuric acid, *d* 1·84) below 20° (cf. Hodgson and Walker, J, 1933, 1620). After 15 mins., the diazo-solution was stirred into a suspension of cuprous oxide (1 g.) in ethyl alcohol (50 c.c.), the temperature being finally raised to 70°. When the cooled solution was poured into water (500 c.c.), 2 : 4-*dichloro-5-nitronaphthalene* (1·7 g.) separated as a brown solid which, twice crystallised from 80% aqueous acetone, formed almost colourless parallelepipeds, m. p. 116·5° (Found : Cl, 29·1. $C_{10}H_5O_2NCl_2$ requires Cl, 29·3%).

2-*Chloro-5-nitronaphthalene*, obtained by diazotisation of 5-nitro-2-naphthylamine in nitrosylsulphuric–glacial acetic acid (cf. Hodgson and Walker, *loc. cit.*) and subsequent treatment with cuprous chloride in concentrated hydrochloric acid, crystallised from aqueous acetone (charcoal) in colourless needles, m. p. 100·5° (Found : N, 6·9. $C_{10}H_6O_2NCl$ requires N, 6·7%).

Bromination of 5-Nitro-1-naphthylamine.—2-*Bromo-5-nitro-1-naphthylamine* was prepared by the gradual addition at 50° of 7 c.c. of a solution of bromine (1 c.c.) in dry chloroform (9 c.c.) to a well-stirred solution of 5-nitro-1-naphthylamine (3 g.) in dry chloroform. The precipitated hydrobromide was converted into the amine by grinding with 5% aqueous ammonia. It is necessary to use slightly less than the calculated amount of bromine for monobromination, otherwise dibromination takes place to some extent. 2-Bromo-5-nitro-1-naphthylamine crystallised from ethyl alcohol in bright orange-red, felted needles, m. p. 121·5° (Found : N, 10·65. $C_{10}H_7O_2N_2Br$ requires N, 10·5%). 2-*Bromo-5-nitroaceto-1-naphthalide* crystallised from aqueous acetic acid in cream needles, m. p. 139° (Found : N, 9·0. $C_{12}H_9O_3N_2Br$ requires N, 9·0%).

2-*Bromo-5-nitronaphthalene* was obtained by submitting 2-bromo-5-nitro-1-naphthylamine to the diazotisation–deamination procedure described above. From the extract of the solid product by boiling acetone, 2-bromo-5-nitronaphthalene separated on cooling; it crystallised from 90% acetone–10% ethyl alcohol (charcoal) in almost colourless needles or plates, m. p. and mixed m. p. with an authentic specimen prepared from 5-nitro-2-naphthylamine, 95·5° (Found : N, 5·6. $C_{10}H_6O_2NBr$ requires N, 5·5%). The mixed m. p. with 1-bromo-8-nitronaphthalene was 55—60°.

2 : 4-*Dibromo-5-nitro-1-naphthylamine.*—5-Nitro-1-naphthylamine (3 g.) was brominated as described above, 8 c.c. of the bromine solution being used. The hydrobromide which separated was collected and basified, and the product dried, dissolved in dry chloroform (15 c.c.), and stirred with 8 c.c. of the bromine solution, giving another precipitate of hydrobromide, which was washed with chloroform and converted into 2 : 4-*dibromo-5-nitro-1-naphthylamine* (3·2 g.); this crystallised from aqueous acetone in orange plates, m. p. 159·5° (Found : Br, 45·9. $C_{10}H_6O_2N_2Br_2$ requires Br, 45·9%).

2 : 4-*Dibromo-5-nitroaceto-1-naphthalide* crystallised from aqueous acetic acid in white needles, m. p. 230·5° (decomp.) (Found : N, 7·4. $C_{12}H_8O_3N_2Br_2$ requires N, 7·2%).

Mercuration of 5-Nitro-1-naphthylamine.—Hot solutions of 5-nitro-1-naphthylamine (8 g.) in glacial acetic acid (60 c.c.) and of mercuric acetate (14 g.) in glacial acetic acid (30 c.c.) were mixed and, after the reaction abated, heated for 3 hours on the water-bath; after cooling, the *5-nitro-1-naphthylamine-2-mercuriacetate* was washed with and crystallised from glacial acetic acid, forming light brown needles or plates, m. p. above 400° (Found : Hg, 44·6. $C_{12}H_{10}O_4N_2Hg$ requires Hg, 44·9%).

2-*Iodo-5-nitro-1-naphthylamine.*—The above mercuriacetate (5 g.) was made into a paste with water, stirred into a solution of iodine (2·9 g.) in boiling aqueous potassium iodide, and heated on the water-bath for 1 hour. The solid obtained was washed successively with water, dilute aqueous sodium thiosulphate, and water (yield, 3·3 g.) and crystallised twice from glacial acetic acid, giving deep red needles, m. p. 121·5—122·5° (Found : N, 9·0. $C_{10}H_7O_2N_2I$ requires N, 8·9%).

2-*Iodo-5-nitroaceto-1-naphthalide*, obtained by heating the above amine (3·9 g.) with acetic anhydride (8 c.c.) and glacial acetic acid (100 c.c.) for 2 hours on the water-bath, was precipitated (3·1 g.) with water and crystallised twice from aqueous acetic acid, giving almost colourless needles, m. p. 169·5° (Found : I, 34·8. $C_{12}H_9O_3N_2I$ requires I, 35·5%).

2-*Iodo-5-nitronaphthalene.*—A diazotised solution of 2-iodo-5-nitro-1-naphthylamine (3 g.) (Hodgson and Walker's procedure, *loc. cit.*) was run into absolute ethyl alcohol (125 c.c.) and heated on the water-bath for 1 hour; the alcohol was then removed, and excess of water added to precipitate the 2-iodo-5-nitronaphthalene. This was boiled with alcohol (charcoal) (125 c.c.), reprecipitated by water, and crystallised from ether and aqueous alcohol, giving almost colourless plates or needles having a very pale purple tint, m. p. 91·5° (Chudožilov, *Chem. Listy*, 1925, **191**, 187, gives m. p. 89—90°) (Found : I, 42·0. Calc. : I, 42·3%). Yield, 1·3 g.

1 : 2-*Di-iodo-5-nitronaphthalene* was prepared from 2-iodo-5-nitro-1-naphthylamine (2·5 g.), a diazotised solution of which, after treatment with urea, was stirred into saturated aqueous potassium iodide (40 c.c.) at 15°. After an hour, the mixture was diluted with water, and the precipitate (3·2 g.) crystallised once from 90% formic acid and twice from pyridine, forming small, deep brown plates, m. p. 132·5° (Found : I, 59·5. $C_{10}H_5O_2NI_2$ requires I, 59·7%).

Nitration of 5-Nitroaceto-1-naphthalide.—The nitration is described in D.R.-P. 145,191 as giving 4 : 5-dinitroaceto-1-naphthalide. This constitution has now been confirmed by hydrolysis of the product to 4 : 5-dinitro-1-naphthylamine, diazotisation, and deamination by cuprous oxide–ethyl alcohol to give 1 : 8-dinitronaphthalene, m. p. and mixed m. p. with an authentic sample 168·5°; mixed m. p. with authentic 1 : 6-dinitronaphthalene (m. p. 163·5°), 123·5°.

5-Nitro-p-toluenesulphon-1-naphthalide.—5-Nitro-1-naphthylamine (7 g.) was refluxed for 1 hour with *p*-toluenesulphonyl chloride (10 g.) in pyridine (30 c.c.), and the mixture poured into dilute hydrochloric acid (1 : 1). The precipitated *5-nitro-p-toluenesulphon-1-naphthalide* (11 g.), crystallised three times from dilute alcohol (charcoal), formed pale cream plates, m. p. 171° (Found : N, 8·4. $C_{17}H_{14}O_4N_2S$ requires N, 8·5%).

2 : 4 : 5-*Trinitro-p-toluenesulphon-1-naphthalide* was prepared by nitrating the above compound (3 g.) in glacial acetic acid (25 c.c.) with 2 c.c. of a solution of nitric acid (4·25 c.c., *d* 1·5) in glacial acetic acid (5·75 c.c.), and heating the mixture on the water-bath for 5 mins. On cooling, the compound separated in cream needles (2·5 g.), m. p. 206° (decomp.) after recrystallisation from glacial acetic acid (Found : N, 12·9. $C_{13}H_{11}O_8N_4S$ requires N, 12·9%).

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